코로나19 백신 플랫폼 기술 특허분석 용역

[코로나19 DNA 백신 기술에 대한 특허 조사 분석]

2021. 12.

특 허 청

목 차

I. 분석개요 ·····1

II. 특허분석 ·····13

III. 회사별 주요 특허 및 국내진입 현황 ·····23

1. Zydus Cadila (인도) ·····23
2. Inovio Pharmaceuticals(미국) ·····29
3. 소결 ·····87

IV. 코로나19 DNA 백신의 자유기술의 영역 ·····88

V. 결론 및 시사점 ·····92

I. 분석개요

1. COVID-19 바이러스의 특징

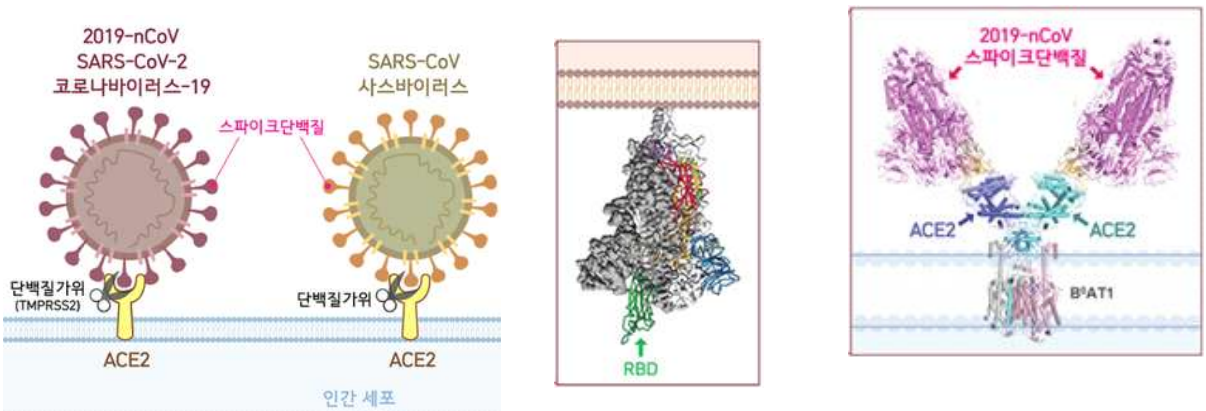
□ COVID-19 발병 원인 및 증세

○ 코로나바이러스감염증-19(COVID-19)는 SARS-CoV-2 감염에 의한 호흡기 증후군으로 병원체인 SARS-CoV-2는 코로나바이러스과(Coronaviridae)에 속하는 RNA 바이러스임

○ 감염 증상으로는 발열, 권태감, 기침, 호흡곤란 및 폐렴 등 경증에서 중증까지 다양한 호흡기 감염증이 나타나며, 그 외에 가래, 인후통, 두통, 객혈과 오심, 설사 등도 나타나는 것으로 알려짐

□ COVID-19의 구조적 특징

○ COVID-19는 ACE2(Angiotensin Converting Enzyme2)'를 수용체로 활용[1]하고, 스파이크 단백질의 일부분이 단백질 가위[2]에 의해 더 쉽게 잘라질 수 있도록 변형이 되어 있기 때문에 사스 바이러스보다 더 빠르게 전염·확산된다고 예상되고 있음



<그림> 좌: COVID-19와 사스바이러스, 우: 스파이크 단백질

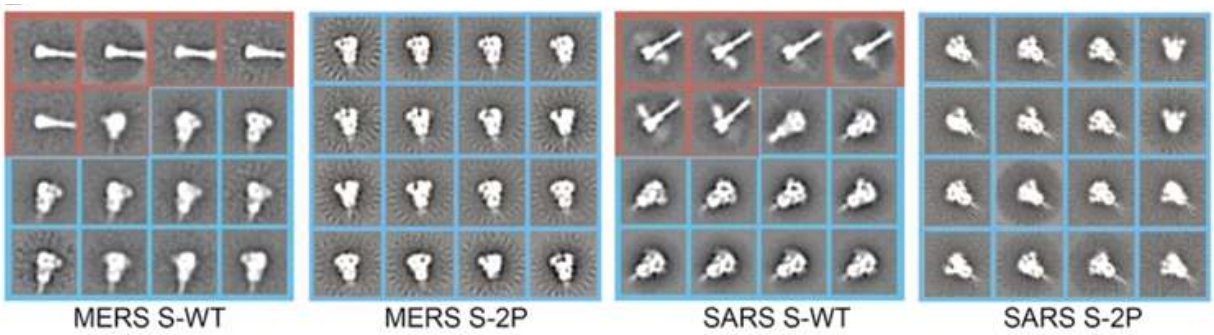
1) Cui et al., 2019
2) Hoffmann et al., 2020

□ 코로나 19 Spike 단백질

○ 코로나 바이러스는 스파이크(S) 단백질을 통해 숙주세포와의 막 융합을 매개함

○ 이는 숙주세포에서 체액성 면역 반응을 일으키기 때문에 주요 백신 표적으로 연구되고 있음

○ 그러나 스파이크 단백질은 인체 세포막과 융합 전 후 구조가 달라져 항체로부터 면역계를 회피하게 됨



<그림> prefusion (blue boxes), postfusion (red boxes) spike protein[3)]

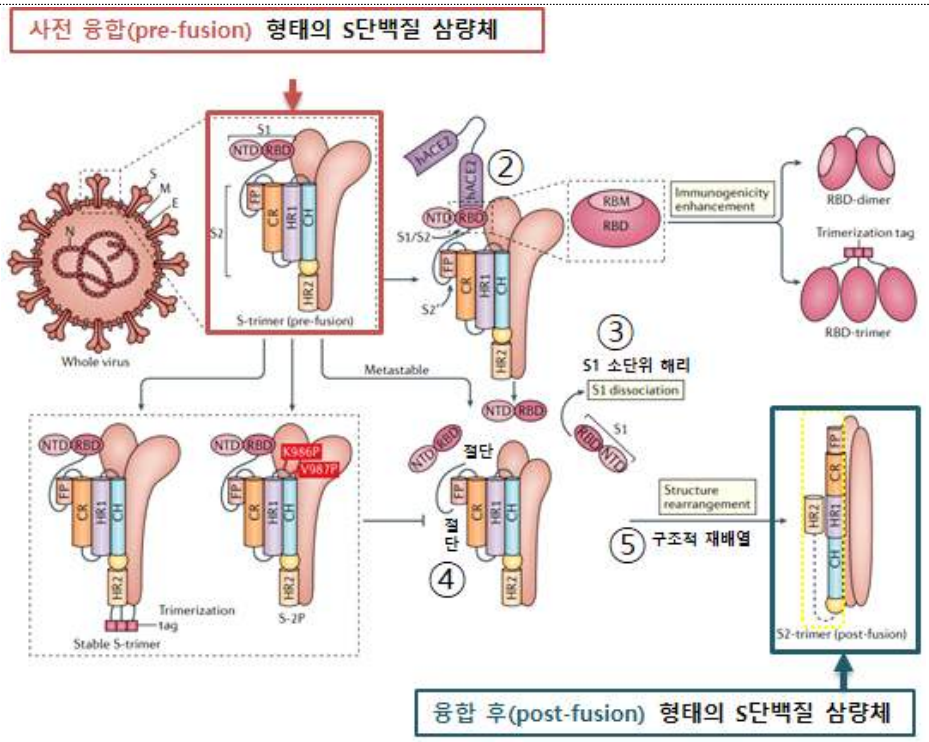
○ 인체 세포막과 융합 전에는 끝이 뭉툭한 형태(pre-fusion, 파란박스) 융합 후 길쭉한 형태(post-fusion, 빨간박스)로 변화

○ S 단백질의 prefusion 형태로 항원 단백질을 안정화시키기 위한 기술이 연구되고 있으며, S-2p mutation을 적용하여 항원 단백질을 최적화함

○ wild type의 경우 prefusion(파란색 상자) 및 postfusion(빨간색 상자) 형태가 모두 관찰되는 반면, S-2p mutatipon을 적용한 경우 prefusion 형태만 확인됨

3) Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen, PNAS August 29, 2017

□ 항원 단백질 최적화



<그림> 사전 융합 전/후 Spike 단백질 삼량체[4)]

① 숙주 세포에 결합하기 전 SARS-CoV-2 S 단백질을 사전 융합(pre-fusion) 형태라고 함

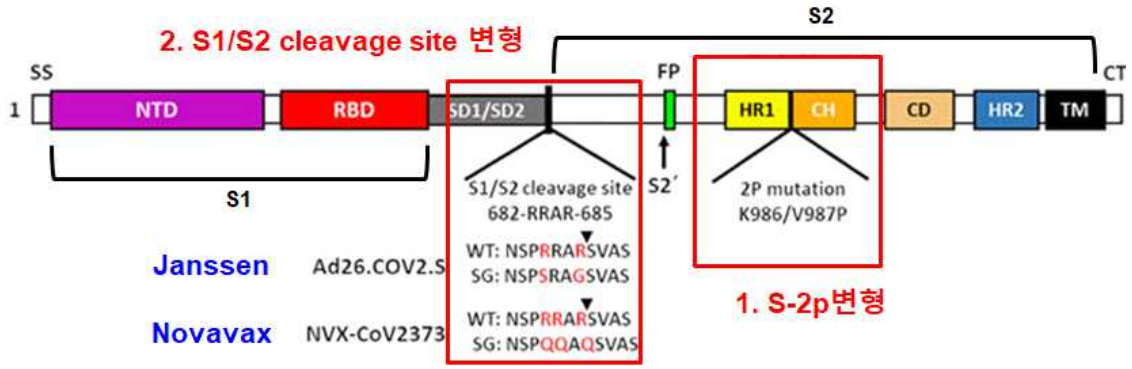
② SARS-CoV-2 S 단백질의 RBD 부위가 숙주 수용체인 이량체 인간 안지오텐신 전환 효소 2(hACE2)에 결합하면

③ S1 소단위의 해리와 ④ S1/S2 및 S2′ 의 절단이 이뤄짐

⑤ **이로 인해 S2 서브유닛의 구조적 재배열이 이뤄지며 융합 후 (post-fusion) 형태의 S단백질 구조가 됨**

4) Viral targets for vaccines against COVID-19, naturereiews immunology, 18 December 2020

5) Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen. PNAS August 29, 2017 114 (35); SARS-CoV-2 Vaccines Based on the Spike Glycoprotein and Implications of New Viral Variants. Front. Immunol., 12 July 2021



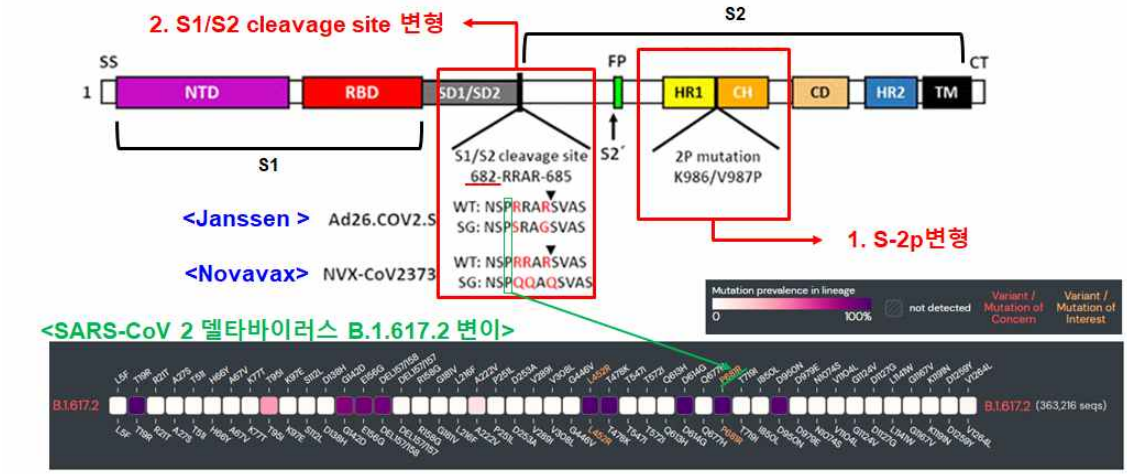
<그림> 얀센과 노바백스의 S protein 항원 design 비교[5)]

Janssen과 Novavax 모두 S-2p 변형과, S1/S2 cleavage site 변형을 적용
다만, S1/S2 cleavage stite 변형 위치가 하기와 같은 차이가 있음
- Janssen: 2개의 아르기닌(R)을 세린(S)과 글라이신(G)로 치환
- Novavax: 3개의 아르기닌(R)을 글루타민(Q)로 치환

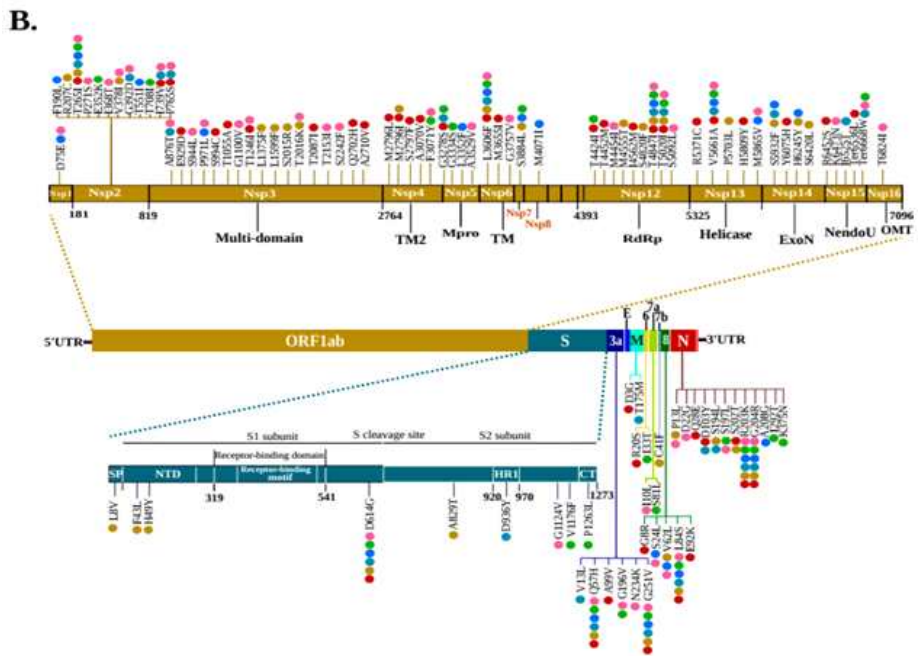
○ **S-2p 변형**: 스파이크 단백질만 분리되면 형태가 불안정해져 모양을 유지하지 못하고 변화하는 특성이 있으며, S 단백질의 2개의 잔기(K986 및 V987)를 프롤린으로 돌연변이 시키면 (S-2P) S 단백질이 안정화되고 사전 융합형태를 유지할 수 있음(얀센, 노바백스, 모더나, 화이자, 큐어백이 S-2p 변형 항원 적용)

○ **S1/S2 cleavage site 변형**: 스파이크 단백질이 둘로 쪼개지는 부분의 아미노산 3개를 '글루타민(Q)'으로 치환으로 s1과 s2가 단백질 분해 효소(protease)에 대한 저항성이 높아져 융합 전 형태의 S 단백질 구조를 유지하게 됨

*사전 융합 형태의 S단백질은 일반적으로 in vitro에서 제조과정 동안 불안정하며, 융합 후 구조 형태로 변형되는 경향이 있음



<그림>얀센과 노바백스의 항원 변형 부위와 델타바이러스의 돌연변이 부위 비교6)



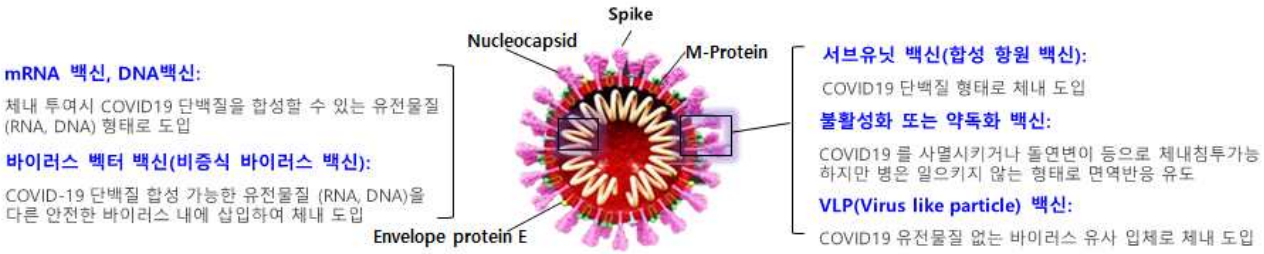
<그림> SARS-CoV-2 게놈 전반의 재발성 돌연변이 분포7)
(출처: '20년 코로나 후속 과제_ 코로나-19 등 바이러스 감염성 질환 관련 백신 분야 변종 대응기술 특허 조사 분석 용역)

6) https://covdb.stanford.edu/page/mutation-viewer/#sec_b-1-617-2
https://outbreak.info/compare-lineages?pango=B.1.617.2&gene=S&threshold=0.2
CORONAVIRUS ANTIVIRAL & RESISTANCE DATABASEA Stanford HIVDB team website. 8/25/2021,

7) Genomic Diversity and Hotspot Mutations in 30,983 SARS-CoV-2 Genomes: Moving Toward a Universal Vaccine for the "Confined Virus"? Pathogens 2020, 9, 829

2. 백신 플랫폼 종류

□ 백신의 플랫폼 기술은 핵산(DNA, RNA) 백신, 바이러스(아데노바이러스) 벡터 백신, 서브유닛(합성항원) 백신, VLP(바이러스 유사 입자) 백신, 불활성화 백신, 약독화 백신 등이 있음



<그림> 백신 플랫폼

<표> - 백신 플랫폼별 특징

백신의 종류	관련 정보	장점	단점	상용화 코로나19 백신	비고
mRNA백신	-	직접 감염원을 다루지 않아 안전성이 높음 신속한 개발 및 생산 가능	불안정성, 생체 내 전달의 비효율성	Moderna (mRNA-1273)	FDA(미국), EMA(유럽) 사용 승인
				Pfizer/ BioNTech (BNT162b2)	FDA(미국), EMA(유럽) 사용 승인
Self amplifying RNA 백신					

백신의 종류	관련 정보	장점	단점	상용화 코로나19 백신	비고
DNA백신	-	직접 감염원을 다루지 않아 안전성이 높음 신속한 개발 및 생산 가능	생체 내 전달의 비효율성 세포핵 내로 이동 필요	-	-
비증식 바이러스 백신 (바이러스 벡터 백신)	인간 대상 허가 백신: 암백신, 에볼라백신(2019 FDA 승인) 등 그 외 유전자치료 벡터	감염성 바이러스를 다룰 필요 없음 우수한 효능	바이러스 벡터 자체에 면역반응형성	AstraZeneca+OxfordUniv (AZD-1222)	EMA(유럽) 사용 승인 FDA(미국) 미승인 상태
				Janssen (Ad26.COV2.S)	FDA(미국),EMA(유럽) 사용 승인
				Serum Institute of India (Covishield)	WHO사용 권장
합성 항원 백신 (서브유닛 백신)	허가된 인간 백신: B형 간염 백신, 폐렴구균 백신 등	감염성 바이러스를 다룰 필요 없음 안전성 우수	면역원성을 높이기 위해 adjuvant 필요	Novarvax (NVX-CoV2373)	FDA(미국) 긴급 사용 승인 신청서 제출 연기
불활성화 또는 약독화 백신	허가된 인간 대상 백신 다수 불활성화 백신-백일해	불활성화 백신-안정성 양호 약독화 백신-효능	불활성화 백신-효능 미흡 약독화	Sinopharm (BBIBP-CorV)	NMPA(중국) 사용 승인

백신의 종류	관련 정보	장점	단점	상용화 코로나19 백신	비고
	백신, 불활화 소아마비 백신 등 약독화 백신-결핵 백신, 경구 소아마비 백신, 홍역 백신, 로타바이러스 백신 등	우수	백신-안전성 이슈		
				Sinovac: (CoronaVac)	NMPA(중국) 사용 승인
VLP(Virus like particle) 백신	허가된 인간 백신: 자궁암 백신 (HPV백신)	다량체 항원 배열 바이러스 입자 구조 유지	최적의 조립 조건 필요	-	-

3. 국내외 mRNA 외 코로나19 백신 플랫폼 기술 개발 동향

□ **(임상현황)** WHO COVID-19 vaccine tracker and landscape. 7월 27일자 자료에 의하면 비증식 바이러스 백신(바이러스 벡터 백신)은 임상 4상, 합성 항원 백신(서브유닛 백신)은 임상 3상, Self amplifying RNA 백신은 임상 2상, DNA 백신은 임상 3상에 진입한 업체가 있는 것으로 조사되었음

○ 비증식 바이러스 백신(바이러스 벡터 백신)에서 임상 4상 백신을 보유한 개발사는 옥스포드/아스트라제네카, 칸시노, 얀센으로 파악됨

○ 합성 항원 백신(서브유닛 백신)에서 임상 2상 백신을 보유한 개발사는 노바백스, Anhui Zhifei Longcom Biopharmaceutical + Institute of Microbiology, Chinese Academy of Sciences, Sanofi Pasteur + GSK, Instituto Finlay de Vacunas, Federal Budgetary Research Institution State Research Center of Virology and Biotechnology "Vector", West China Hospital + Sichuan University, Center for Genetic Engineering and Biotechnology (CIGB), Nanogen Pharmaceutical Biotechnology로 파악됨

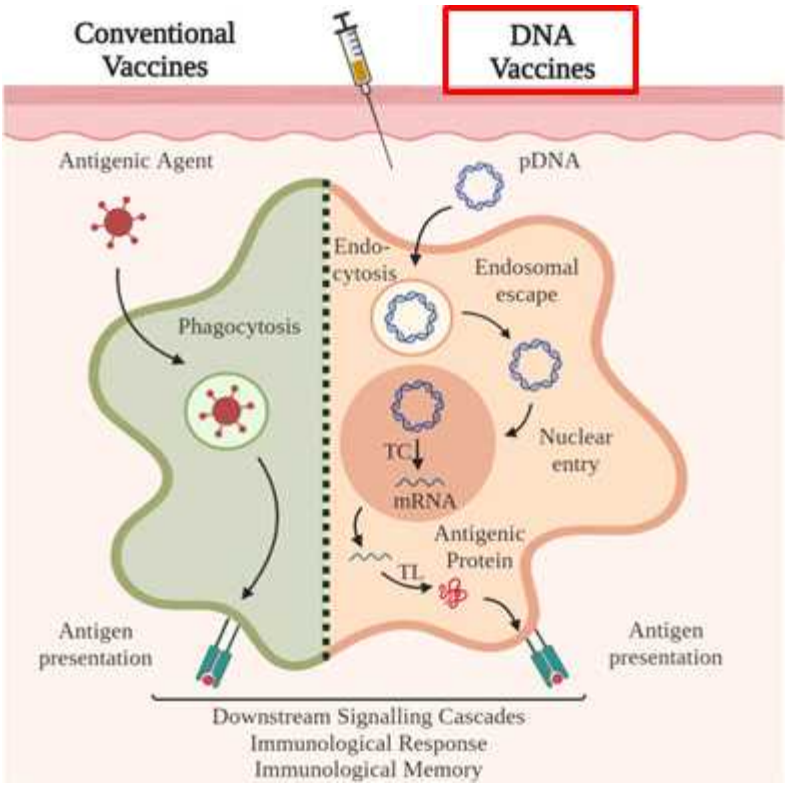
○ Self amplifying RNA 백신에서 임상 2상 백신을 보유한 개발사는 Elixirgen Therapeutics, Inc으로 파악됨

○ DNA 백신에서 임상 3상 백신을 보유한 개발사는 Zydus Cadila, Inovio Pharmaceuticals + International Vaccine Institute + Advaccine (Suzhou) Biopharmaceutical Co., Ltd, AnGes + Takara Bio + Osaka University로 파악됨

□ **(국내현황)** 비증식 바이러스 백신에서 셀리드, 합성항원 백신에서 SK 바이오사이언스, 유바이오로직스, Self amplifying RNA 백신에서 큐라티스, DNA 백신에서 제넥신, 진원생명과학이 개발 중인 것으로 파악됨

4. DNA 백신 플랫폼 기술 개요

□ 기술 개요[8)]



<그림> 기존 백신과 DNA 백신의 차이

○ DNA 백신은 항원 염기서열을 가진 DNA(플라스미드)를 체내 주입 후 전기천공(electroporation) 등의 방법으로 세포 내로 보내고 이후 우리 몸의 세포가 항원 단백질을 생산함

○ 항원 단백질이 체내에서 생성되도록 지시하는 mRNA 백신과 유사 RNA백신은 세포질에 도달하기만 하면 되는 반면, DNA 백신은 세포핵까지 도달해야함

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8) https://m.dongascience.com/news.php?idx=48916
https://onlinelibrary.wiley.com/doi/full/10.1046/j.1365-2796.2003.01140.x?sid=nlm%3Apubmed
https://www.sciencetimes.co.kr/news/%EB%8B%A4%ED%81%AC%ED%98%B8%EC%8A%A4-dna-%EB%B0%B1%EC%8B%A0%EC%9D%B4-%EB%B6%80%EC%A7%84%ED%95%9C-%EC%9D%B4%EC%9C%A0/

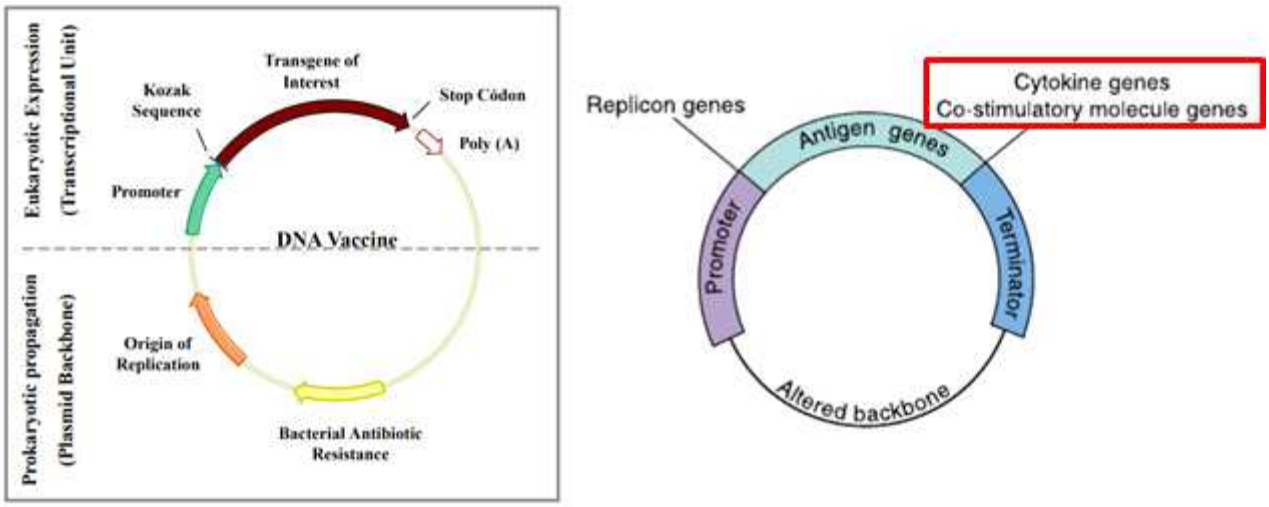
백신플랫폼기술 (Vaccine PlatformTechnologies), KISTEP 기술동향브리프

○ DNA는 이중나선형 형태로 단일가닥인 RNA보다 분자 구조상 안정적이기에 운반과 보관 측면에서 상대적으로 쉽다는 장점이 있음

○ 단점으로는 생체 내 전달의 비효율성으로 효과가 떨어질 수 있으며, 이를 보완할 전달 방법들로 전기천공법(electroporation)이 있음

○ 현재 DNA백신은 주로 말과 같은 동물 백신으로만 활용되고 있고, 인체를 대상으로 한 임상시험에서 잠재적 면역반응을 유도하지 못한 상태이며, 지카바이러스, 메르스 등 백신 개발 과정의 임상이 진행 중임

□ DNA 백신 플라스미드 구조 개략도



<그림> DNA 백신 플라스미드 구조[9)]

○ 진핵 세포에서 관심 항원의 발현을 담당하는 전사단위로 프로모터, 항원, 정지코돈 및 poly(A)로 구성되어 있음

○ 박테리아 세포에서 증식 및 백신 플라스미드 유지를 담당하는 원핵생물 복제 기점과 selectable marker로 구성

9) *DNA vaccines: a review, Journal of Internal Medicine 2003; 253: 402–410*
DNA Vaccines Approach: From Concepts to Applications, January 2014World Journal of Vaccines 04(02):50-71

○ 또한, DNA 백신의 효능을 높이기 위해 사이토카인 또는 공동-자극 분자를 코딩하는 유전자 추가하거나, 바이러스 복제 효소를 암호화하는 유전자 추가함

□ **DNA 백신 임상 현황 (출처: WHO COVID-19 vaccine tracker and landscape. 21.7.27일 자료)**

No.	Phase	Type of candidate vaccine	Developers	국가
1	3	nCov vaccine	ZydusCadila	인도
2	2/3	INO-4800+electroporation	Inovio Pharmaceuticals + International Vaccine Institute + Advaccine (Suzhou) Biopharmaceutical Co., Ltd	미국, 국제기구, 중국
3	2/3	AG0301-COVID19	AnGes + Takara Bio + Osaka University	일본, 일본, 일본
4	1/2	GX-19N	Genexine Consortium	국내기업
5	1/2	GLS-5310	GeneOne Life Science, Inc.	국내기업

○ 임상 3상 이상으로 진행된 DNA 백신 개발사인 ZydusCadila (인도)와 주요 시장국 미국 개발사 Inovio Pharmaceuticals(미국) + International Vaccine Institute(국제기구) + Advaccine (Suzhou) Biopharmaceutical Co., Ltd(중국)를 중심으로 특허 분석을 실시함

II. 특허분석

1. 특허분석 개요

□ 과제목적

○ 코로나19 DNA 백신 플랫폼별 또는 공정별 주요기업의 보유 특허 분포 및 기술의 분석을 통해 국내기업이 필요로 하는 세부기술(특허포트폴리오)을 파악

○ 코로나19 백신 플랫폼별 필수적인 요소기술에 대한 특허권의 독점적인 효력이 미칠 수 없는 자유기술의 영역(public domain)을 확인

□ 과제범위 및 내용

○ 코로나19 DNA 백신을 개발하고 있는 기업 중 개발단계에서 선두그룹[10]에 해당되는 주요기업의 기술개요, 환경분석(기술분석, 기업현황, 보유 파이프라인, 개발동향, 임상 현황, 논문분석), 주요특허 분석을 통해 시사점을 도출함

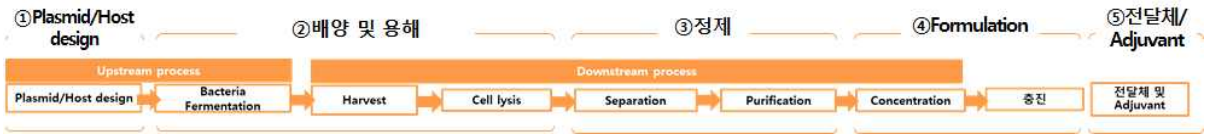
○ 코로나19 DNA 백신 플랫폼별 필수적인 요소기술 관련 원천특허

10) 비증식 바이러스 백신, 합성항원 백신 - 임상 3상 이상, self-amplifying RNA 백신 -임상1/2상, DNA 백신 - 2/3상 이상

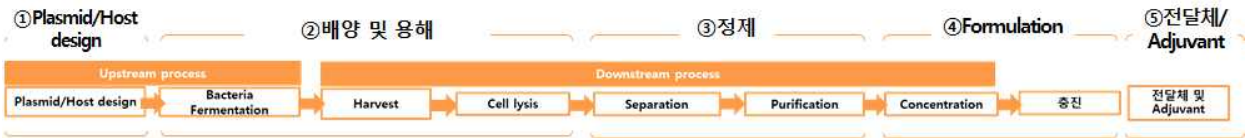
2. 공정별 주요 특허 분석

□ DNA 백신 공정 개요

○ DNA 백신 제조공정을 ❶ Plasmid/design, ❷ 배양 및 용해, ❸ 정제, ❹ formulation ❺전달체/ Adjuvant 으로 세분하고 각 공정에 따른 특허를 분석함



[DNA 백신 플랫폼 특허 분석 결과 요약]



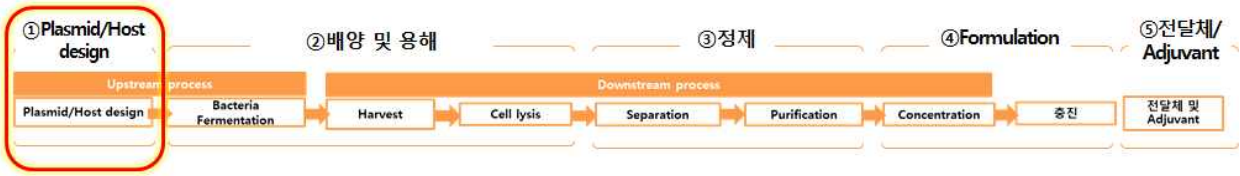
※청색글자 표기: 코로나19 백신 관련 특허

공정	세부공정	ZydusCadila	INOVIO*	합계
①Plasmid/Host design	Plasmid (벡터설계)	-	US9669091 WO2015-054012 WO2016-054003 WO2016-153995	4
	Plasmid (항원설계)	WO2021-214703	WO2021-173829	2
②배양 및 용해	Cell lysis	-	WO2008-148010	1
③정제	Separation, Purification	-	WO2008-148010	1
④Formu lation	전달효율 향상	-	US7491537 WO2009-065121	2
⑤전달체/ Adjuvant	전달체	- -	US6752781 US7054685 US6883222 WO2003-059952 EP1480720 WO2004-004825 US7717874 US7442182 US7922709 US7664545 US7547293 US10369359 US7942845 WO2008-048632 US7931640 WO2009-045813 US8617099 WO2010-121160 US10045911 US10610684 WO2011-109399 WO2011-109406 WO2011-137221 WO2013-066427 WO2013-019603 WO2017-112898 WO2017-117251 WO2017-117273 WO2017-117508 US2020-0016400	31

			WO2021-189012	
총계		1	40	41

INOVIO* : 공동개발사 Advaccine의 코로나19 항원 설계 관련 문헌 CN 112626090 외 4건 후단 참조

[공정별 개발사별 주요특허 국가별 분포 현황_①Plasmid/Host design]

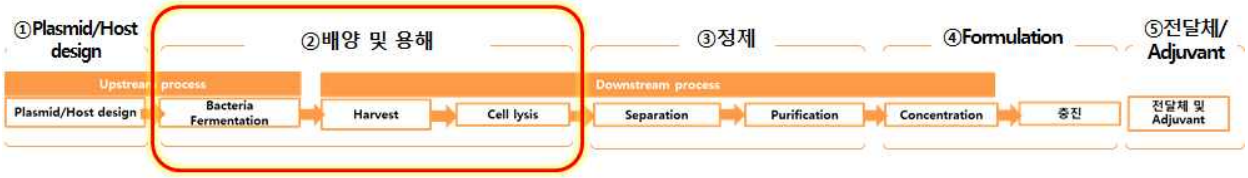


※청색글자 표기: 코로나19 백신 관련 특허

※녹색글자 표기: 자유기술의 영역 참고

세부공정	개발사	대표문헌	세부기술	PCT	KR	US	JP	EP	CN	기타	비고
pDNA 준비 (벡터 설계)	INOVIO	US9669091	IL-23	O	O	O	O	O	O	O	면역원성 증가
		WO2015-054012	IL-33	O	O	O	O	O	O	O	면역원성 증가
		WO2016-054003	IL-21	O	O	O	O	O	O	O	면역원성 증가
		WO2016-153995	CD40 리간드	O	O	O	O	O	O	O	면역원성 증가
pDNA 준비 (항원 설계)	Zydus cadila	WO2021-214703	IgE 또는 tPA 시그널 서열 +SARS-CoV-2 spike protein 서열	O						O	**발현 벡터 pVAX1 (자유실시 기술)** [DNA 플라스미드 제조공정 실시예 13 참조]
	INOVIO	WO2021-173829	IgE 리더 서열 + S full length gene	O		O					**발현 벡터 pGX0001 (자유실시 기술)** 진핵생물내 발현 향상과 면역원성 향상 Inovio의 독점적인 in silico 유전자 최적화 알고리즘 사용,

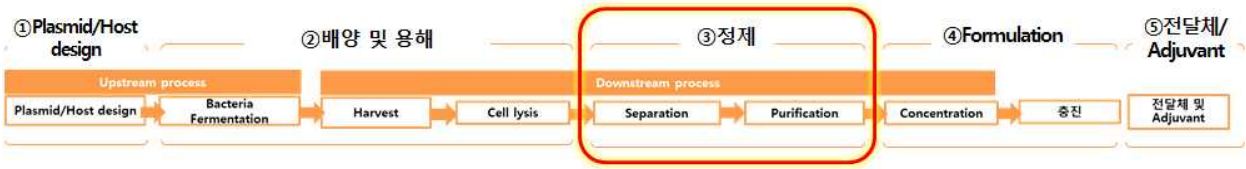
[공정별 개발사별 주요특허 국가별 분포 현황_②배양 및 용해]



※청색글자 표기: 코로나19 백신 관련 특허

세부 공정	개발사	대표문헌	세부기술	PCT	KR	US	JP	EP	CN	기타	비고
Cell lysis	INOVIO	WO2008-148010	고농도 플라스미드 DNA 제조 공정	O	O	O	O	O	O	O	bubble mixer

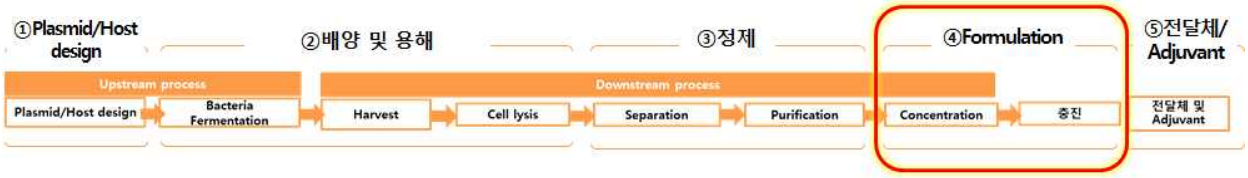
[공정별 개발사별 주요특허 국가별 분포 현황_③정제]



※청색글자 표기: 코로나19 백신 관련 특허

세부 공정	개발사	대표문헌	세부기술	PCT	KR	US	JP	EP	CN	기타	비고
Separation, Purification	INOVIO	WO2008-148010	고농도 플라스미드DNA 제조 공정	O	O	O	O	O	O	O	bubble mixer

[공정별 개발사별 주요특허 국가별 분포 현황_④Formulation]



※청색글자 표기: 코로나19 백신 관련 특허

세부공정	개발사	대표문헌	세부기술	PCT	KR	US	JP	EP	CN	기타	비고
전달 효율 향상	INOVIO	WO2009-065121	poly glutamic acid	O	O	O		O	O	O	DNA 플라스미드 안정성 증가
		US7491537	poly glutamic acid	O		O	O	O	O	O	전기천공 보조, 형질감염 증가

[공정별 개발사별 주요특허 국가별 분포 현황_⑤전달체/Adjuvant]

※청색글자 표기: 코로나19 백신 관련 특허

세부공정	개발사	대표문헌	세부기술	PCT	KR	US	JP	EP	CN	기타	비고
전달체	INOVIO	US6752781	전기천공 관련 기술			O					
		US7054685	〃	O		O		O		O	
		US6883222	〃	O		O	O	O		O	
		WO2003-059952	〃	O	O	O	O	O	O	O	
		EP1480720	〃	O		O		O		O	
		WO2004-004825	전기 천공 장치와 인젝션 장치	O		O	O	O	O	O	
		US7717874	전기천공 관련 기술	O		O	O	O		O	
		US7442182	〃	O		O					
		US7922709	〃	O		O	O	O		O	
		US7664545	핀전극 배열을 가진 정전류 시스템	O		O		O		O	분산패턴으로중첩지점 방지,조직손상최소화
		US7547293	전기천공 관련 기술	O		O		O			
		US10369359	〃	O	O	O	O	O	O	O	
		US7942845	〃	O		O		O			
		WO2008-048632	〃	O	O	O	O	O	O	O	
		US7931640	〃	O	O	O	O	O	O	O	
		WO2009-045813	〃	O		O					
		US8617099	〃	O		O	O	O	O	O	
		WO2010-121160	〃	O	O	O		O		O	
		US10045911	〃	O		O		O	O	O	
		US10610684	〃	O	O	O	O	O	O	O	
		WO2011-109399	〃	O	O	O		O		O	
		WO2011-109406	〃	O	O	O	O	O	O	O	
		WO2011-137221	〃	O	O	O		O	O	O	
		WO2013-066427	〃	O	O	O	O	O	O	O	
		WO2013-019603	〃	O		O					
		WO2017-112898	〃	O	O	O	O	O	O	O	
		WO2017-117251	〃	O	O	O	O	O	O	O	
		WO2017-117273	〃	O	O	O	O	O	O	O	
		WO2017-117508	〃	O	O	O	O	O	O	O	
		US2020-0016400	〃	O	O	O	O	O	O	O	
		WO2021-189012	〃	O		O					

3. 지재권 분쟁 현황

□ (VGXI) 진원생명과학은 2008년 미국의 VGXI사를 인수하였는데 VGXI사는 ALDEVRON사와 세포 파쇄 장치인 기포 혼합기(bubble mixer) 기술 관련 특허에 대해 미국에서 1건이 특허 분쟁 중임

[VGXI DNA 백신 관련 주요특허 분쟁현황]

특허권자	청구인	관련기술	대상특허	결론	주요국 출원여부
VGXI	ALDEVRON	②배양 및 용해	US 7238522 B2 (WO2004-108260 A2)	진행중	미국O, 유럽O, 일본X, 한국X

[VGXI DNA 백신 관련 주요 특허 분쟁 청구범위]

(US 7238522 B2) Claim 1. An apparatus for isolating cellular component of interest from cells comprising:

(a) a first tank, wherein the first tank is used for holding a suspension of cells having the cellular component of interest;

(b) a mixer in fluid communication with the first tank;

(c) a second tank in fluid communication with the mixer, wherein the second tank is used for holding a lysis solution;

(d) a holding coil in fluid communication with the mixer; and

(e) a bubble-mixer chamber with a top and a bottom having:

(i) a first inlet in fluid communication with the holding coil;

(ii) a second inlet in fluid communication with a third tank, wherein the third tank is used for holding a precipitation solution, a neutralization solution, or a mixture thereof;

(iii) a third inlet in fluid communication with a gas source;

(iv) a vent; and

(v) an outlet in fluid communication with a fourth tank, wherein the fourth tank is used for separating precipitated cellular components from fluid cell lysate;

wherein, the mixer is a high-shear, low-residence-time-mixing-device, wherein the residence-time is less than or equal to about one second; the suspension of cells having the plasmid DNA from the first tank is allowed to flow into the mixer; the lysis solution from the second tank is allowed to flow into the mixer; a lysate-mixture is allowed to flow from the mixer into the holding coil; the lysate-mixture from the holding coil is allowed to flow into the bubble-mixer chamber; the precipitation solution, the neutralization solution, or the mixture thereof from the third tank is allowed to flow into the bubble-mixer chamber; and a suspension containing the cellular component of interest is allowed to flow from the bubble-mixer chamber into the fourth tank.

4. 라이선스(LICENSE) 현황

□ **(세포파쇄, 전달체 - 디바이스)** 진원생명과학은 2008년 미국의 VGXI사를 인수하여 고농도 고순도의 플라스미드 DNA 생산에 필요한 정제의 핵심기술인 AirMix 기술 관련 특허를 보유하게 되었음

[전달체 관련 특허출원 현황]

세부기술	국제출원	미국	유럽	일본	국내 진입
세포파쇄	WO2019-232324	US 2021-0207075 A1	EP 3802781 A1	JP 2021-525521 A	O
세포파쇄, 분리, 정제	WO2008-148010 A9	US2020-0017819 A US 2009-0004716 A1	EP 2153260 B1	JP 5793726 B2	O

(EP 2153260 B1) Claim 1. A large scale process for producing high purity samples of low copy number plasmids from bacterial cells, comprising the steps of:a) producing a lysate solution by contacting a cell suspension of said bacterial cells comprising said low copy number plasmids with lysis solution; b) neutralizing said lysate solution with a neutralizing solution to produce a dispersion that comprises neutralized lysate solution and debris and wherein the dispersion fluid is held for less than one hour to separate the neutralized lysate solution; c) filtering the dispersion through at least one filter; d) performing ion exchange separation on said neutralized lysate solution to produce an ion exchange eluate; and e) performing hydrophobic interaction separation on said ion exchange eluate to produce a hydrophobic interaction solution;wherein step a) comprises mixing said cell suspension with lysis solution in a high shear, in-line mixer;
wherein step b) comprises mixing said lysate solution with said neutralizing solution in a bubble mixer; and
wherein step e) comprises performing hydrophobic interaction separation using a hydrophobic interaction column or a hydrophobic interaction membrane to form a hydrophobic interaction solution;
wherein the method comprises transitioning from one step to a subsequent step substantially continuously.

(JP 5793726 B2) 청구항 1 박테리아 세포로부터의 고순도 시료 DNA 플라스미드를 제조하기 위한 대규모 방법으로서, 이하의 공정 :a) 복수의 세포 세포 현탁액을 용해액(lysis solution)과 접촉하는 것에 의한 용균액(lysate solution)을 제조해;
b) 중화액을 이용하여 상기 용균액을 중화하여 중화한 용균액과 잔해물을 포함한 분산액을 제조해; c) 적어도 하나의 필터를 통과시켜 분산액을 여과해; d) 상기 중화한 용균액에 대해서 이온

교환 분리를 해서, 이온 교환 용출액을 제조해; e) 상기 이온 교환 용출액에 대해서 소수성 상호작용 분리를 하고, 소수성 상호작용 컬럼에서 용출된 용액을 제조하는 것을 포함하고 여기서 상기 공정 a)는 강한 전단력이 가해지는 인라인 믹서- 안에서 상기 세포 현탁액과 용해액을 혼합하는 것을 포함하고 및 상기 공정 b)는 버블 믹서 중에서 상기 용균액과 상기 중화 용액을 혼합하는 것을 포함한, 상기 방법.

III. 회사별 주요 특허 및 국내진입 현황

1. Zydus Cadila (인도)

1) 환경분석[11]

○ 인도 제약사 Zydus Cadila (자이더스 캐딜라)는 1952년 설립되었으며, Cadila Healthcare로도 불림

○ Zydus Cadila의 백신 기술 센터 (VTC)에서 디프테리아, 백일해, 파상풍, B형 헤모필루스 인플루엔자, 인유두종 바이러스, 말라리아, 출혈성 콩고열, 에볼라 및 일본뇌염 백신 개발 파이프라인을 보유 중임

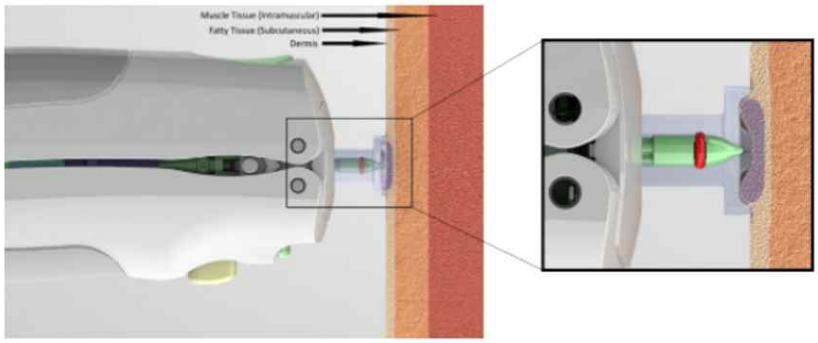
○ Zydus Cadila사는 인도 최초의 4가 비활성화 인플루엔자 백신인 VaxiFlu-4를 자체적으로 개발, 제조 및 출시한 이력을 가지고 있음

○ 2021년 8월 20일 세계 첫 DNA 기반의 코로나19 백신으로 **자이코브디(ZyCoV-D)**를 개발했으며, 인도에서 긴급사용승인 받음

<그림> Zydus Cadila 코비드 19 백신 Zycov-D

11) *https://m.dongascience.com/news.php?idx=48916*
https://www.mkhealth.co.kr/news/articleView.html?idxno=53050
https://pharmajet.com/tropis-id/
https://cnews.pinpointnews.co.kr/view.php?ud=20210908083750503cd1e7f0bdf_45
https://www.edaily.co.kr/news/read?newsId=03401366629244080&mediaCodeNo=257&OutLnkChk=Y

○ **자이코브디**는 다른 코로나19 백신과 달리, 무바늘 주입 장치로 피부에 강력하고 미세한 물줄기를 쏴 DNA를 세포까지 효과적으로 전달하는 특징을 가짐. 접종 시 통증이 없기 때문에 어린이들도 쉽게 맞을 수 있음



<그림> PharmaJet의 바늘 없는 주사 장치 Tropis[12)]

○ **무바늘 주입 장치는 미국 파마제트(Pharma Jet)사의 고속분사 주사시스템 'tropis 를 이용해 접종함**. 이는 DNA 백신 개발에 대부분 활용되는 근육 내 투여방식이 아닌, **피부 내 투여 방식으로 근육보다 면역세포가 풍부한 피부 아래 조직을 타겟**하여 **DNA의 효율적 전달이 가능함**

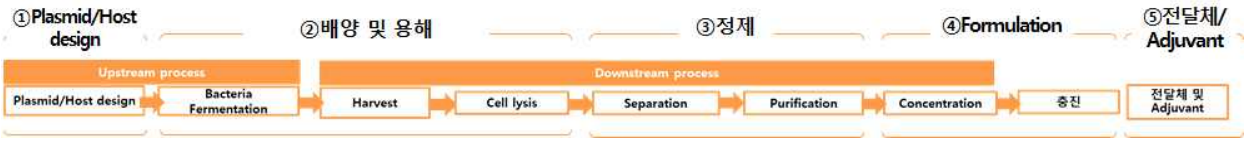
○ 자이코브디 1차 접종 후 28일차와 56일차에 각각 2차, 3차 접종을 해야 함

○ 국내 엔지켐생명과학은 자이더스 캐딜라와의 코로나19 백신 생산 공급 관련하여, 글로벌 생산 공급 의향서를 체결한 바 있음. 현재 위탁생산 및 라이선스 계약의 세부조항 등과 계약 실행에 대한 구체적인 사전 절차를 진행하고 있으나 계약 여부는 확정되지 않았다고 발표함 (21.11.09)

12) *https://pharmajet.com/tropis-id/*

2) 특허 분석 결과

[Zydus Cadila 주요 특허 요약]



※청색글자 표기: 코로나19 백신 관련 특허

공정	세부공정	세부기술	문헌번호	건수 (대표문헌기준)
①Plasmid/Host design	Plasmid/Host design (벡터설계)	-	-	-
	Plasmid/Host design (항원설계)	• IgE 또는 tPA 시그널 서열 +SARS-CoV-2 spike protein 서열	WO2021-214703	1
②배양 및 용해		-	-	-
③정제		-	-	-
④Fomulation		-	-	-
⑤전달체/ Adjuvant		-	-	-

○ Zydus Cadila는 코로나19 백신 기술 관련하여 pDNA 기술 중 항원 설계 기술을 보유하고 있는 것으로 파악되었음

○ Zydus Cadila의 코로나19 백신 기술 관련 특허 중 국내 진입한 특허는 없는 것으로 파악되었음

1. WO2021-214703 A1					
서지사항					
발명의 명칭	A VACCINE AGAINST SARS-COV-2 AND PREPARATION THEREOF		현재상태	공개	
출원번호 (출원일)	PCT-IB2021-053321 (2021.04.22.) (우: 2020.04.23)	등록•공개번호 (등록•공개일)	WO2021-214703 A1(2021.10.28)		
출 원 인	CADILA HEALTHCARE LIMITED(IN)	패밀리 특허	-		
발명자	PATEL, Pankaj(IN)	공정분류	Plasmid/ Host design (항원설계)	세부 기술	IgE 또는 tPA 시그널 서열 +SARS-CoV-2 spike protein 서열
상세사항					
요약	The current invention provides a DNA construct comprising S gene or S1 gene region of 2019-nCoV spike-S protein. The DNA construct of the present invention comprises DNA plasmid vector carrying S gene or S1 gene region of 2019-nCoV spike-S protein. The vector may further comprise a gene encoding IgE signal peptide or a gene encoding t-PA signal peptide. The DNA construct according to the present invention is further used in the preparation of an immunogenic composition or a vaccine for treating or preventing corona virus or its related diseases.				
청구항1 (대표 청구항)	A **DNA construct** comprising a gene encoding **S protein** of **SARS-CoV-2** or a **truncated** gene of **S protein of SARS-CoV-2** optionally with a gene encoding **signal peptide**.				
청구항2 (종속항)	The **truncated** gene of **S protein** of SARS-CoV-2 as claimed in claim 1 is **S1** region or a receptor binding domain **RBD** that binds to the human angiotensin converting enzyme- 2(ACE-2) receptor.				
청구항3 (종속항)	A **vector** comprising a gene encoding **S protein of SARS-CoV-2 orS1** region of S protein of SARS-CoV-2 optionally with a gene encoding **signal peptide**.				
청구항4 (종속항)	The **vector** as claimed in claim 3 further comprising **regulatory element(s)** required for the **expression** of S gene of SARS-CoV-2 or S1 region of S gene of SARS-CoV-2.				
청구항5 (종속항)	The **vector** as claimed in claim 3 further comprising human cytomegalovirus immediate-early (CMV) promoter, bovine growth hormone (**BGH**) **polyadenylation signal**, **kanamycin resistance gene** or suitable **combination** thereof.				
청구항6 (종속항)	The **vector** as claimed in claim 3 is selected from **pVAX1,** pCDNA 3.1, pCDNA 4.0, pCMV and PCAGG.				
청구항7 (종속항)	The **signal peptide** as claimed in claim 1 or claim 3 is **IgE signal peptide** or t-PA signal peptide.				
청구항12 (종속항)	The DNA construct or **vector** as claimed in any preceding claim is **injected** by a **needle-free injection** or by an electroporator system.				

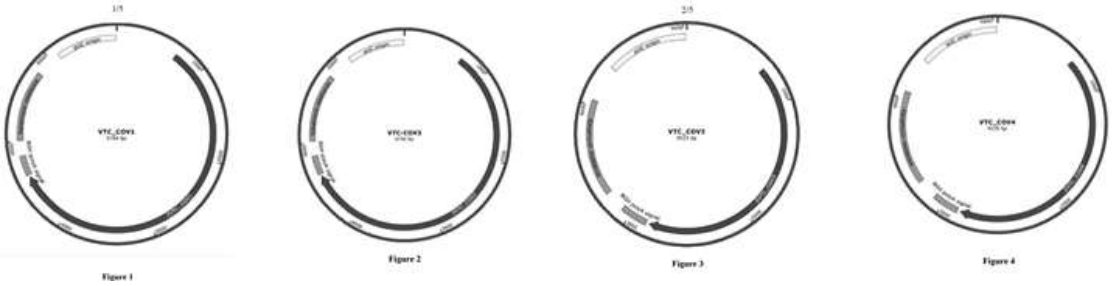
청구항16 (종속항)	The gene **encoding S protein of SARS-CoV-2** as claimed in claim 1, expresses S protein of SARS-CoV-2 wherein S protein of SARS-CoV-2 has **proline** substitution selected from **K986P**, **V987P**, **F817P**, **A892P**, **A899P**, **A942P** and suitable combinations thereof. <참고> 변이 위치 *출처: SEC-MALS Validated SARS-CoV-2 Prefusion Trimeric Spike Variant Proteins*
청구항22 (종속항)	The **DNA construct** as claimed in any preceding claim is **produced** by scalable production process using **batch or fed-batch** method with suitable media compositions comprising of yeast extract, tryptone, glycerol and other suitable ingredients available for high density **E. coli** culture. Also, temperature range from **30 °C to 42 °C** can be used according to the present invention to **increase plasmid yield** from bacterial biomass.
청구항23 (종속항)	The DNA construct as claimed in any preceding claim is **purified** by the purification **process** comprising one or more of the following steps: (a) **lysis** of host cell containing plasmid DNA; (b) **clarifying** the lysate by filtration to obtain clarified lysate; (c) treating **lysate** to **removeendotoxin** and other impurities; (d) **purifying** the treated solution of step (c) with **plasmidDNA** using one or more of the **chromatography** techniques selected from **affinity chromatography (AC), ion exchange chromatography (IEC) and / or hydrophobic interaction chromatography (HIC)**; (e) **concentrating** the purified plasmid comprising of one or more following steps of (i) precipitation , (ii) diafiltration and / or (iii) lyophilization.
분석내용	• 본 발명은 SARS-CoV-2 S 단백질을 항원으로하는 DNA 백신에 관한 것임 **[실시예 1: SARS-CoV-2의 전장 S 유전자 또는 S1 유전자의 합성 또는 분리]** [0130] • 전장 S 유전자(서열번호 1) 과 S1 영역(서열번호 2)의 아미노산 서열은 NCBI(MN908947.2.)기반으로 설계됨 • 인간 발현 코돈 최적화하고, 독일 Gene Art에 의해 화학적으로 합성 **[실시예 2: 상기 유전자 서열에 IgE 또는 t-PA 시그널 펩타이드를 코딩하는 벡터 제작]** 1. **하기 4개의 서열을 pVAX1(Invitrogen, USA)** 벡터에 삽입하여, 4개의 벡터 제작 ZVTC_COV1 **(도1)**, ZVTC_COV2 **(도2)**, ZVTC_COV3 **(도3)**, ZVTC_COV4 **(도4)**

① IgE 리더 서열 + 전장 S 유전자 (서열번호: 3(아미노산) 및 서열번호: 4(핵산)) => 동물 면역화 실험

② t-PA 리더 서열 + 전장 S 유전자 (서열번호: 5 및 서열번호: 6)

③ IgE 리더 서열+ S1 영역 유전자 (서열번호: 7 및 서열번호: 8)

④ t-PA 리더 서열 +S1 영역 유전자 (서열번호. : 9 및 SEQ ID No.: 10)



2. 플라스미드 DNA 작제물은 DH5-a에서 형질전환 후 배양 후 miniprep 플라스미드 분리 키트를 사용하여 플라스미드 분리

✓ 동일한 방식으로, **2P 치환 또는 hexaPro 치환을 갖는 SARS-CoV-2의 S 단백질**을 코딩하는 **플라스미드 DNA** 작제물이 실시예 1 및 2에 예시된 방법에 따라 제조될 수 있음 (안정화된 S 단백질 프리퓨전을 부호화하는 유전자)
1. SEQ ID NO.: 11 - Amino acid sequence of **full-length S gene (Hexapro)** with **IgE leader** sequence
2. SEQ ID NO.: 13 - Amino acid sequence of **full-length S gene (2P)** with **IgE leader** sequence

[실시예 13: DNA 플라스미드 제조공정] [0168]

a) 세포 용해

1. 세포의 용해는 0.2M NaOH 및 1% SDS를 포함하는 용액을 사용하여 화학적 방법으로 수행
2. 용해된 배양액의 pH를 대략 pH 5 - 13으로 조정
3. 세포 용해물을 연속 유동 원심분리 또는 심층 여과(depth filtration)에 의해 정화(clarified)

b) 정제 (purification)

1. 용해 후, 냉각된 아세트산칼륨 완충액을 첨가하여 용액의 pH를 약 pH 5.5에서 중화
2. RNA 불순물을 제거하기 위해 $CaCl_2$를 첨가
3. UF/DF에 의한 buffer exchange 수행
4. 정화된 용해물을 100 - 500 kDa MWCO(kilo Dalton molecular weight cutoff) 필터를 사용하여 정용여과(diafiltered)
5. 음이온 교환 컬럼 (weak anion resin) 정제
6. 추가로 음이온 교환 용리는 TFF에서 100 - 500 kDa 컷오프 카세트를 사용하여 정용여과

2. Inovio Pharmaceuticals(미국) + International Vaccine Institute (국제 백신연구소) + Advaccine (Suzhou) Biopharmaceutical (중국)

1) 환경분석[13]

○ 미국의 Inovio Pharmaceuticals은 HPV, 암 및 전염병과 관련된 질병으로부터 치료 및 예방을 위한 DNA 의약품 개발을 선도하고 있는 생명공학 기업임

○ 1979년 설립되었으며, 2008년 7월 VGX Pharmaceuticals와 합병함

○ Inovio 의 코로나 19 후보 백신은 INO-4800 으로 불리는 DNA 백신플랫폼이며, 정밀하게 설계된 DNA플라스미드를 독자적인 스마트 device인 CELLECTRA 2000로 투여함

○ Inovio는 중국의 과학자들이 2020년 1월 코드비 19 유전자 염기서열을 공개한지 **불과 3시간만에 자사의 SynCon시스템으로 백신 후보서열을 찾아냄 (컴퓨터 알고리즘을 사용하여 백신을 디자인)**

○ 중국과 한국에서 각각 INO-4800의 임상 시험을 진행하기 위해 Advaccine(중국) 및 International Vaccine Institute(국제백신연구소, IVI)와 협약함

○ 2020년 6월 3일 국제백신연구소는 국내 식품의약품안전처로부터 이노비오의 코로나19 백신 후보물질 'INO-4800'의 국내 임상 1상과 2상 시험을 승인받았다고 밝힘

○ 중국에서는 INO-4800 과 중국의 시노백이 개발한 코로나 백신 '코로나백'(coronaVac)을 교차 접종하는 '이종 프라임-부스

13) https://www.datanami.com/2020/03/23/can-ai-find-a-cure-for-covid-19/
http://www.medisobizanews.com/news/articleView.html?idxno=80678
https://www.ivi.int/ko/ivi-inovio-and-knih-to-partner-with-cepi-in-a-phase-i-ii-clinical-trial-of-inovios-covid-19-dna-vaccine-in-south-korea/
https://www.inovio.com/dna-medicines-pipeline/
http://m.yakup.com/index.html?m=n&mode=view&nid=257191

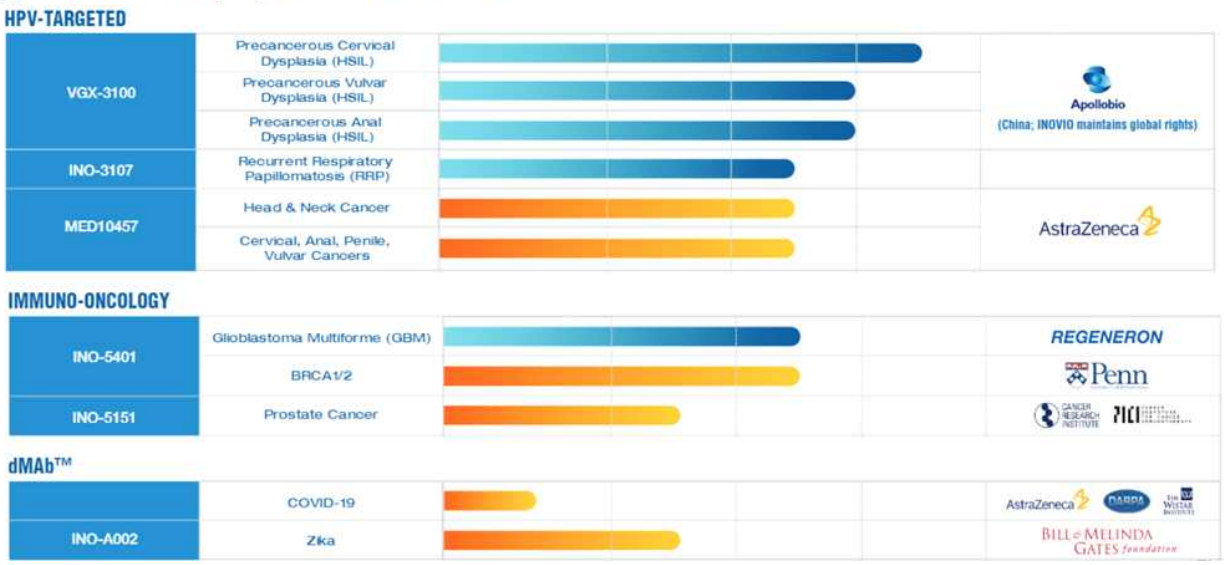
트'(heterologous prime-boost) 임상 시험 2건을 승인 받음 (21.08.10)

○ 2020년 4월 Inovio는 COVID-19 백신 후보인 INO-4800의 1상 시험을 시작했음

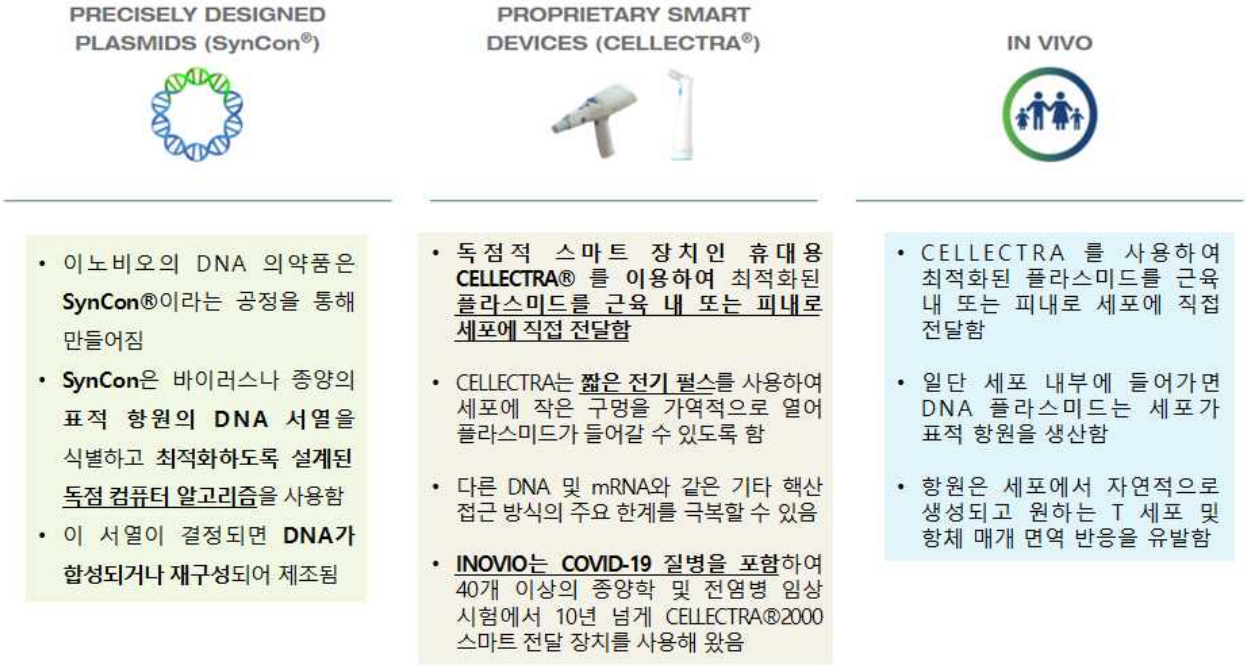
<그림> INOVIO의 코로나19 백신 관련 파이프라인

○ INO-4802: 미래에 발생할 수 있는 변이들로부터 감염을 예방하도록 설계된 '코로나19' 변이 범용백신으로, 전임상 결과, 특정 균주에 대응하는 백신들에 비해 다수의 변이들에 대해 폭넓고 높은 중화항체 생성을 유도한 것으로 나타남

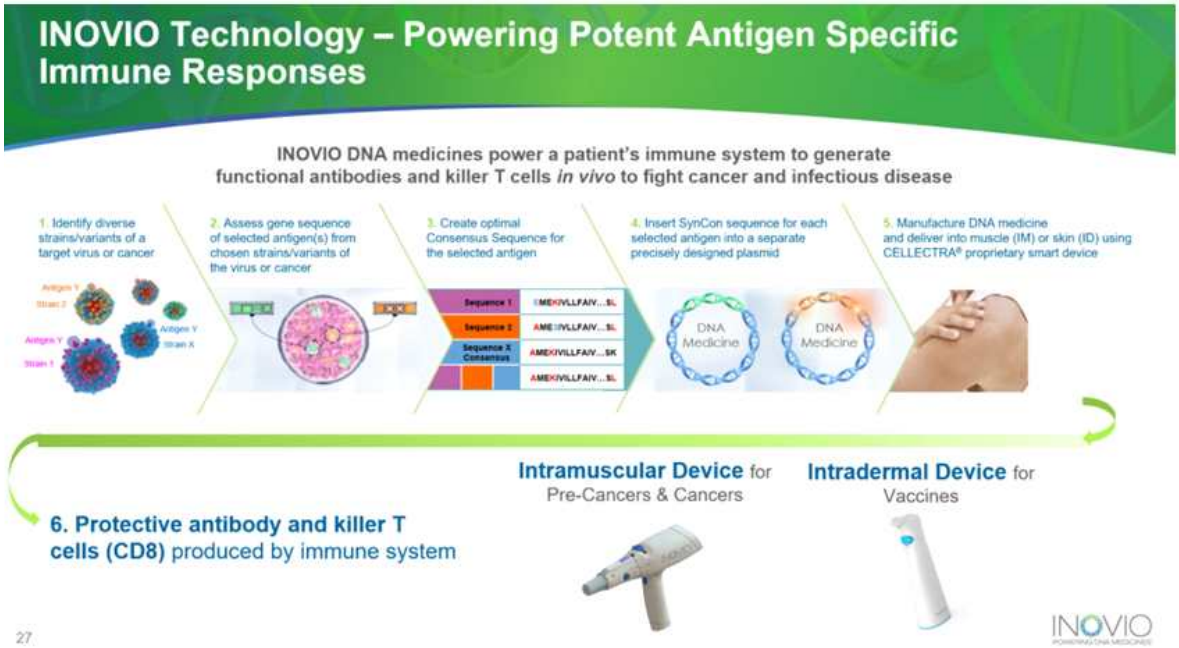
○ 코로나19 범용백신 후보물질을 만들어 내기 위해 2020년 10월부터 브라질, 캐나다, 인도, 이탈리아, 나이지리아, 남아프리카공화국, 영국, 미국 및 일본 등 여러 지역에서 4개월여에 걸쳐 돌연변이 서열을 확인하고, 변이들로부터 일련의 중복 변이(overlapping mutation)들을 파악함



<그림> INOVIO DNA 의약품 파이프라인



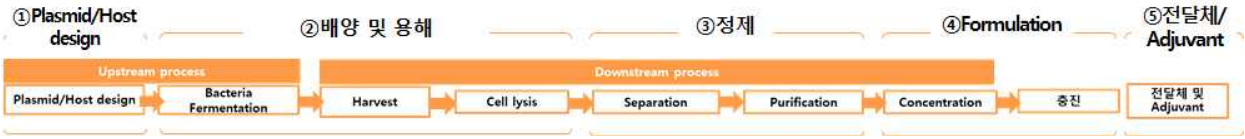
<그림> INOVIO의 DNA 의약품 관련 기술: 플라스미드 최적화 설계& 전달기기



<그림> INOVIO의 DNA 백신 개발 과정

2) 특허 분석 결과

[INOVIO 주요 특허 요약]



※청색글자 표기: 코로나19 백신 관련 특허

공정	세부공정	세부기술	문헌번호	건수 (대표문헌기준)
①Plasmid/Host design	Plasmid(벡터설계)	• IL-23 • IL-33 • IL-21 • CD40 리간드	US9669091 WO2015-054012 WO2016-054003 WO2016-153995	4
	Plasmid(항원설계)	• IgE 리더 서열 + S full length gene	**WO2021-173829**	1
②배양 및 용해	Cell lysis	• 고농도 플라스미드 DNA 제조 공정	WO2008-148010	1
③정제	Separation, Purification	• 고농도 플라스미드 DNA 제조 공정	WO2008-148010	1
④Fomulation	Formulation (전달효율향상)	• poly glutamic acid	US7491537 WO2009-065121	2
⑤전달체/ Adjuvant	전달체	• 전기 천공 장치와 인젝션 장치 • 핀전극 배열을 가진 정전류 시스템	US6752781 US7054685 US6883222 WO2003-059952 EP1480720 WO2004-004825 US7717874 US7442182 US7922709 US7664545 US7547293 US10369359 US7942845 WO2008-048632 US7931640 WO2009-045813 US8617099 WO2010-121160 US10045911 US10610684 WO2011-109399 WO2011-109406 WO2011-137221 WO2013-066427 WO2013-019603 WO2017-112898 WO2017-117251 WO2017-117273 WO2017-117508 US2020-0016400 WO2021-189012	31

[INOVIO 국내 진입 특허]

공정	PCT 공개번호	PCT 출원일	공개번호(KR)	발명의 명칭	우선권출원일
①	WO2014-151279	2014-03-13	10-2015-0128900	항원 및 어쥬번트로서 인터류킨-23을 갖는 백신	2013-03-15
①	WO2015-054012	2014-10-02	10-2016-0066033	어쥬번트로서 인터류킨-33을 갖는 백신	2013-10-07
①	WO2016-054003	2015-09-29	10-2017-0062467	항원 및 어쥬번트로서 인터류킨-21을 갖는 백신	2014-10-01
①	WO2016-153995	2016-03-18	10-2017-0129804	CD40 리간드를 어쥬번트로서 갖는 백신	2015-03-20
②, ③	WO2008-148010	2008-05-23	10-2010-0017884	고농도의 생물학적 활성 분자 함유 조성물 및 그 제조 방법	2007-05-23
④	WO2009-065121	2008-11-17	10-2010-0098634	폴리-Ｌ-글루타메이트를 포함시킴으로써 안정성이 증가된 ＤＮＡ 제형	2007-11-16
⑤	WO2001-085202	2001-05-04	10-2001-0005932	약물과 핵산의 골격 근육 내 주입 장치 및 방법	2000-05-05
⑤	WO2003-059952	2003-01-16	10-2004-0099264	근육내 투여를 위한 이중특이성 항체 ＤＮＡ 작제물	2002-01-18
⑤	WO2008-048632	2007-10-17	10-2009-0107014	포유류의 세포의 전기천공용 전기천공 장치 및 이의 사용 방법	2006-10-17
⑤	WO2008-143988	2008-05-16	10-2008-0110988	싱글-니들 생체내 일렉트로포레이션용 장치	2007-05-18
⑤	WO2009-091578	2009-01-16	10-2010-0106583	가변성 전류 밀도 단일 바늘 전기 천공 시스템	2008-01-17
⑤	WO2010-121160	2010-04-16	10-2017-0136021	비접촉식 전기천공 전극 및 방법	2009-04-16
⑤	WO2011-109406	2011-03-01	10-2013-0020662	참을 수 있는 그리고 최소 침습적인 피부 전기천공 장치	2010-03-01
⑤	WO2011-109399	2011-03-01	10-2013-0025874	다수의 조직 층 전기천공 애플리케이터 및 장치	2010-03-01
⑤	WO2011-137221	2011-04-28	10-2019-0020187	구강 점막 전기천공 장치 및 그 용도	2010-04-28
⑤	WO2013-066427	2012-06-28	10-2020-0123864	최소 침습 피부 전기천공 장치	2011-06-28
⑤	WO2017-112898	2016-12-22	10-2018-0098591	전력 스위치가 달린 배터리 팩을 가진 전기천공 디바이스	2015-12-22
⑤	WO2017-117273	2016-12-28	10-2018-0099748	진피내 제트 주입 전기천공 디바이스	2015-12-28
⑤	WO2017-117251	2016-12-28	10-2018-0099747	개선된 신호 발생기를 가진 전기천공 디바이스	2015-12-28
⑤	WO2017-117508	2016-12-30	10-2018-0099751	락-아웃 시스템으로 분리가능한 바늘 어레이를 갖는 전기천공 디바이스	2015-12-30
⑤	WO2018-057900	2017-09-22	10-2019-0055155	전기천공을 사용하여 지방 조직의 생체내 형질감염을 최소로 침습성으로 하기 위한 방법 및 장치	2016-09-23

- INOVIO는 코로나19 백신 기술 관련하여 pDNA 기술 중 항원설계 기술을 보유하고 있는 것으로 파악되었음
- INOVIC의 코로나19 백신뿐만 아니라 다른 질병에 적용가능한 전기천공 기술 관련 특허 대부분이 국내에 진입한 것으로 파악되었음
- INOVIO는 Advaccine와 공동개발을 하고 있고, Advaccine의 코로나19 항원 설계 관련 문헌으로 CN 112626090 외 4건이 확인됨(후단 참조)

1. US 9669091 B2

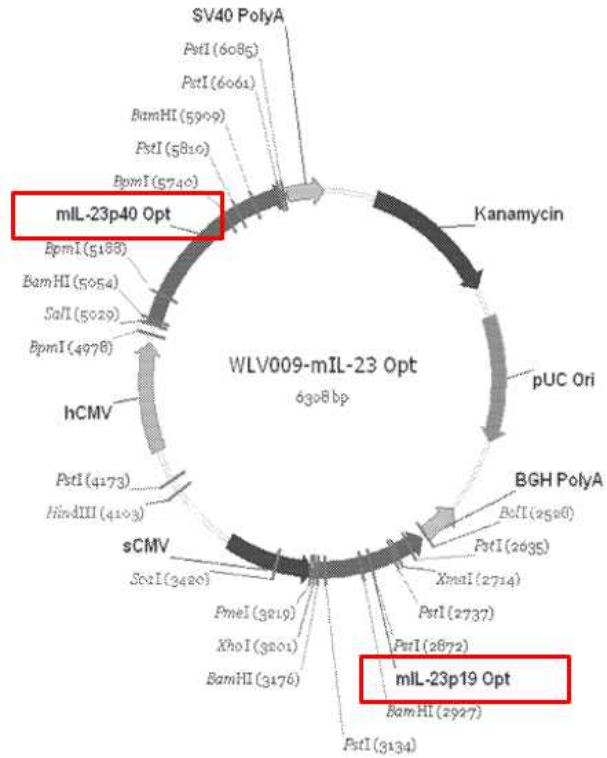
서지사항

발명의 명칭	Vaccines having an antigen and interleukin-23 as an adjuvant		현재상태	공개	
출원번호 (출원일)	US 14/775087 (2014.03.13.) (우: 2013.03.15)	등록•공개번호 (등록•공개일)	US 9669091 B2 (2017.06.06)		
출 원 인	INOVIO PHARMACEUTICALS THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA(US)	패밀리 특허	WO 1건 | KR 1건 | EP 1건 | JP 1건 | CN 1건 | 기타 3건		
발명자	David B. Weiner(US) Jian Yan(US) Matthew Morrow(US) 외 2명	공정분류	Plasmid/ Host design	세부 기술	IL-23

상세사항

요약

Disclosed herein is a vaccine comprising an antigen and IL-23. Also disclosed herein are methods for increasing an immune response in a subject. The methods may comprise administering the vaccine to the subject in need thereof.



청구항1 (대표 청구항)	A **vaccine** comprising **one or more nucleic acid sequences** that **encode an antigen** and **Interleukin-23 (IL-23)** comprising **p19 subunit and p40 subunit**, wherein **p19 subunit of IL-23 is encoded** by a nucleic acid that is 95% identical or greater to the nucleotide sequence as set forth in **SEQ ID NO:22** and wherein **p40 subunit of IL-23** is encoded by a nucleic acid that is 95% identical or greater to the nucleotide sequence as set forth in **SEQ ID NO:23.**
청구항2 (종속항)	The method of claim 9, wherein **administering** the vaccine includes **electroporation**
분석내용	• 면역 반응을 증가시키는 안전하고 더욱 효과적인 아쥬반트가 필요하며, 본 발명에서는 **IL-23을 발현 벡터 내에 삽입**하여 면역원을 강화함 • **IL-23의 아단위인 P19와 p40 를 인코딩하는 핵산의** 코돈 최적화한 형태임

2. WO2015-054012 A1

서지사항

발명의 명칭	VACCINES WITH INTERLEUKIN-33 AS AN ADJUVANT		현재상태	공개	
출원번호 (출원일)	PCT-US2014-058727 (2014.10.02)	등록•공개번호 (등록•공개일)	WO2015-054012 A1 (2015.04.16)		
출 원 인	THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA(US) INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	US 3건 | KR 1건 | JP 1건 | EP 1건 | CN 2건 | 기타 6건		
발명자	WEINER, David(US) VILLARREAL, Daniel(US) MORROW, Matthew(US) 외 1명	공정분류	Plasmid/ Host design	세부 기술	IL-33

상세사항

요약

Disclosed herein is a vaccine comprising an antigen and IL-33. Also disclosed herein is a method for increasing an immune response in a subject. The method may comprise administering the vaccine to the subject in need thereof.

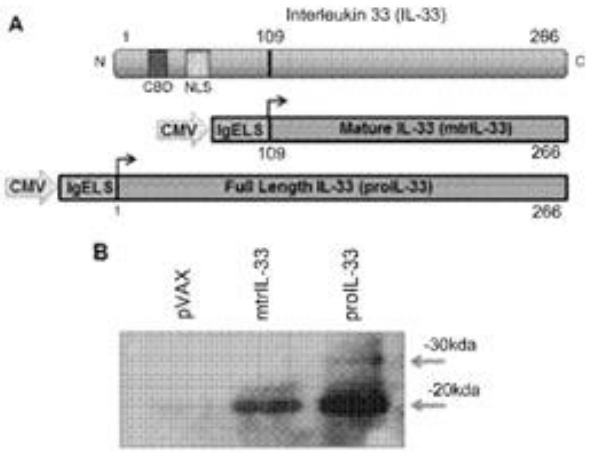


FIG. 1

청구항1 (대표 청구항)

A vaccine comprising an antigen and IL-33.

청구항2 (종속항)	The vaccine of claim 1, wherein IL-33 is encoded by a nucleotide sequence selected from the group consisting of: a nucleotide sequence having at least about 95% identity to a nucleotide sequence as set forth in SEQ ID NO: 1, a nucleotide sequence as set forth in SEQ ID NO: 1, a nucleotide sequence having at least about 95% identity to a nucleotide sequence as set forth in SEQ ID NO:3, and a nucleotide sequence as set forth in SEQ ID NO:3.
청구항22 (종속항)	The method of claim 21, wherein administering the vaccine includes electroporation.
분석내용	• 면역 반응을 증가시키는 안전하고 더욱 효과적인 아쥬반트가 필요하며, 본 발명에서는 IL-33을 **발현 벡터 내에 삽입**하여 면역원을 강화함 • IL-33은 CBD와 NLS가 없는 성숙한 형태(mature)로 존재할 수 있으며 mature형태의 IL-33은 **면역 반응을 조절하는 전염증성 사이토카인**으로 작용할 수 있음

3. WO2016-054003 A1

서지사항

발명의 명칭	VACCINES HAVING AN ANTIGEN AND INTERLEUKIN-21 AS AN ADJUVANT		현재상태	공개	
출원번호 (출원일)	PCT-US2015-052884 (2015.09.29) (우: 2014.10.01)	등록•공개번호 (등록•공개일)	WO2016-054003 A1 (2016.04.07)		
출 원 인	THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA(US) INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	US 3건 | KR 1건 | JP 2건 | EP 1건 | CN 1건 | 기타 4건		
발명자	WEINER, David, B.(US) MORROW, Matthew, P.(US)	공정분류	Plasmid/ Host design	세부 기술	IL-21

상세사항

요약

Disclosed herein is a vaccine comprising an antigen and IL-21. Also disclosed herein are methods for increasing an immune response in a subject. The methods may comprise administering the vaccine to the subject in need thereof.

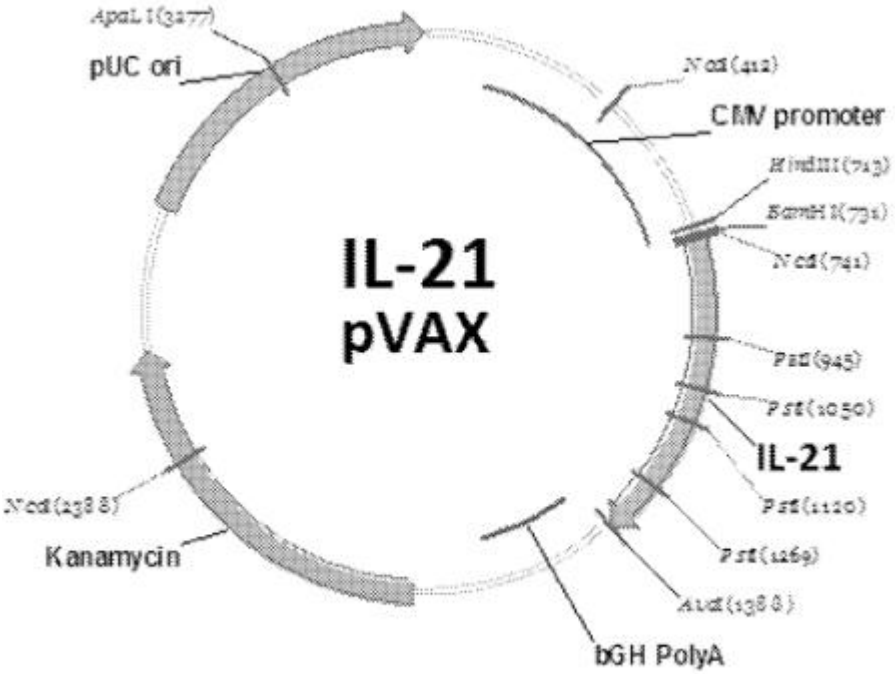


Figure 1

청구항1 (대표 청구항)	A **vaccine** comprising an **antigen** and **IL-21**
청구항2 (종속항)	The vaccine of claim 1, wherein **IL-21 is encoded** by a nucleotide sequence selected from the group consisting of: a nucleotide sequence having at least about 95% identity to a nucleotide sequence as set forth in **SEQ ID NO:3** and a nucleotide sequence as set forth in SEQ ID NO:3.
청구항15 (종속항)	The method of claim 14, wherein administering the vaccine includes **electroporation**.
분석내용	• 면역 반응을 증가시키는 안전하고 더욱 효과적인 아쥬반트가 필요하며, 본 발명에서는 **IL-21을 발현 벡터 내에 삽입**하여 면역원을 강화함

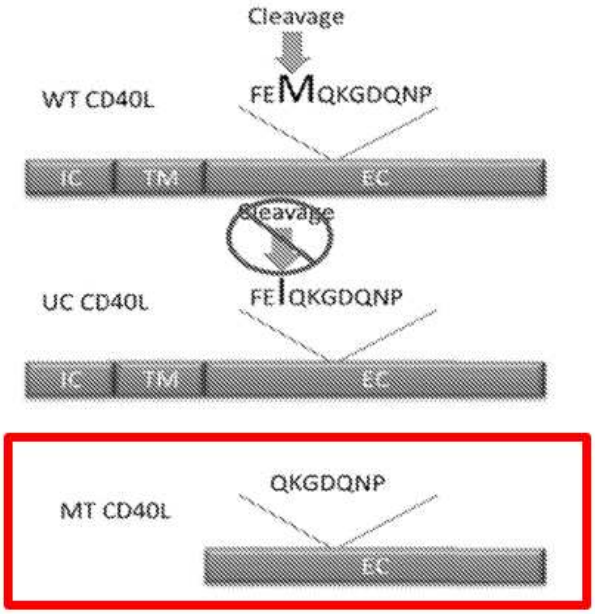
4. WO2016-153995 A1

서지사항

발명의 명칭	VACCINES WITH CD40 LIGAND AS AN ADJUVANT		현재상태	공개	
출원번호 (출원일)	PCT-US2016-023126 (2016.03.18) (우: 2015.03.20)	등록•공개번호 (등록•공개일)	WO2016-153995 A1 (2016.09.29)		
출 원 인	THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA(US) INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	US 1건 | KR 1건 | EP 1건 | CN 1건 | 기타 5건		
발명자	WEINER, David(US) MORROW, Matthew(US) WISE, Megan(US)	공정분류	Plasmid/ Host design	세부 기술	CD40 리간드

상세사항

요약	Disclosed is a vaccine comprising **an antigen and CD40L**, wherein the antigen may be encoded **by a first nucleic acid** and **CD40L** may be encoded by a **second nucleic acid.** Also disclosed are methods for increasing an immune response in a subject, the methods comprise administering the vaccine to the subject in need thereof. Further disclosed is the antigen selected from the group consisting of a **human papilloma virus (HPV) antigen, a human immunodeficiency virus (HIV) antigen, an influenza antigen, and a Plasmodium falciparum antigen.**
청구항1 (대표 청구항)	A **vaccine** comprising a **first nucleic acid sequence** encoding an **antigen**, or an immunogenic fragment thereof and a **second nucleic acid sequence** encoding a **CD40L**, or an immunogenic fragment thereof, wherein the second nucleic acid sequence encoding a **CD40L** comprises at least 90% identity to the nucleic acid sequence of **SEQ ID NOS: 1, 3, 5, 7, 9 or 11**.

분석내용	• **CD40L(리간드)**을 아쥬반트로서 이용함으로써 개체에서 항원에 대한 면역 반응을 증가시키는 백신 • CD40L (서열 번호: 1, 3, 5, 7, 9, 11)는 인터페론-γ (IFN-γ), 종양 괴사 인자 알파 (TNF-α), 인터류킨-2 (IL-2) 생산을 증가시켜 **근육과 피부 조직 둘 모두에서 면역 반응을 증대시킬 수 있음** • CD40L 벡터는 도면 1a에 도시된 바와 같이 함께 또는 별도로 플라스미드 내에 배열될 수 있음 • HPV 항원 + 와일드 타입에 비해, **HPV항원 + MT 타입으로 면역화된 생쥐에서 TNF-α 값이 더 높음을 확인함** 

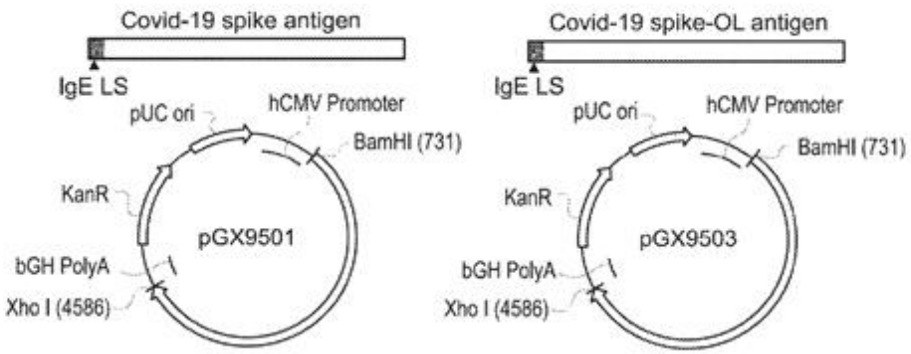
5. WO2021-173829 A1

서지사항

발명의 명칭	VACCINES AGAINST CORONAVIRUS AND METHODS OF USE		현재상태	공개	
출원번호 (출원일)	PCT-US2021-019662 (2021.02.25)	등록•공개번호 (등록•공개일)	WO2021-173829 A1 (2021.09.02)		
출 원 인	Inovio Pharmaceuticals, Inc. (US) The Wistar Institute of Anatomy and Biology (US)	패밀리 특허	US 1건		
발명자	YAN, Jian(US) BRODERICK, Kate(US) WEINER, David(US) 외 2명	공정분류	Plasmid/ Host design	세부 기술	IgE 리더 서열 + S full length gene

상세사항

요약	Disclosed herein are <u>nucleic acid molecules encoding a SARS-CoV-2 spike antigen,</u> SARS-CoV-2 spike antigens, immunogenic compositions, and vaccines and their use in inducing immune responses and protecting against or treating a Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) infection in a subject.
청구항 1 (대표 청구항)	A **nucleic acid** molecule encoding a Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) spike antigen, the nucleic acid molecule comprising: a nucleic acid sequence having at least about 90% identity over an entire length of the nucleic acid sequence set forth in nucleotides 55 to 3837 of **SEQ ID NO: 2;** a nucleic acid sequence having at least about 90% identity over an entire length of SEQ ID NO: 2; the nucleic acid sequence of nucleotides 55 to 3837 of SEQ ID NO: 2; the nucleic acid sequence of SEQ ID NO: 2; a nucleic acid sequence having at least about 90% identity over an entire length of **SEQ ID NO: 3**; the nucleic acid sequence of SEQ ID NO: 3; a nucleic acid sequence having at least about 90% identity over an entire length of nucleotides 55 to 3837 of SEQ ID NO: 5; a nucleic acid sequence having at least about 90% identity over an entire length of **SEQ ID NO: 5**; the nucleic acid sequence of nucleotides 55 to 3837 of SEQ ID NO: 5; the nucleic acid sequence of SEQ ID NO: 5; a nucleic acid sequence having at least about 90% identity over an entire length of **SEQ ID NO: 6**; or the nucleic acid sequence of SEQ ID NO: 6.
청구항2 (종속항)	An **expression vector** comprising the nucleic acid molecule according to claim 1.
청구항10 (종속항)	The method of any one of claims 7 to 9, wherein administering comprises at least one of **electroporation** and **injection**.

분석내용	• 본 발명은 SARS-CoV-2 스파이크 항원을 인코딩하는 DNA 백신에 관한 것임 • [SARS-CoV-2 DNA 백신 작제물의 설계 및 합성] • GISAID(Global Initiative on Sharing All Influenza Data)에서 게시된 4개의 SARS-CoV-2 전체 게놈 서열로부터 4개의 스파이크 단백질 서열을 검색 • 스파이크 단백질 시퀀스가 100% 일치한 세 개의 서열을 (Covid-19 스파이크 항원, 서열 번호 1)로 했으며, 남은 하나는 다른 시퀀스와 98.6% 동일성을 나타내는 서열을 outlier (Covid-19 스파이크-OL 항원, 서열 번호 4)로 함 • SARS-CoV-2 항원의 면역원성을 증가시키기 위해 각 서열의 N-말단에 IgE 리더 서열을 추가 • 진핵생물에서의 발현 향상과 면역원성을 향상시키기 위해 Inovio의 독점적인 in silico 유전자 최적화 알고리즘을 사용하여 SARS-CoV-2 IgE-spike를 인코딩하는 최적화된 DNA 서열 생성 • 발현 벡터 pGX0001에 클로닝 (human cytomegalovirus immediate-early promoter, bovine growth hormone polyadenylation signal를 포함하고 있는 벡터 pGX0001.) • 상기 클로닝을 통해 생성된 플라스미드는 pGX9501 및 pGX9503으로 지정했으며, pGX9501을 이후 INO-4800으로 명명  FIG. 1A <도 1A> SARS-CoV-2 합성 DNA 백신 구축의 개략도 SARS-CoV-2 spike 단백질 항원 앞에 IgE leader sequence가 삽입되어 있는 형태 • INO-4800의 면역원성은 CELLECTRA¢ç 전달 장치를 사용하여 전달, CELLECTRA¢ç 장치는 CELLECTRA 2000¢ç 장치 또는 CELLECTRA¢ç 3PSP 일 수 있음 (Cellectra¢ç 장치 및 시스템은 미국 특허 제7,245,963호에 기술되어 있음) • 형질 전환 촉진 에이전트는 poly-L-glutamate 이고, poly-L-glutamate는 6 mg/ml이하의 농도라고 기재되어 있음 • INO-4800의 마우스 및 기니피그, 원숭이, 건강한 지원자에 대한 면역원성 평가 실시예를 보유하고 있음

- [1261] pGX9501에 삽입된 서열

pGX9501의 DNA 삽입 서열(서열번호: 2)(IgE 리더 서열 밑줄):

```
1     ATGGATTGGA CTTGGATTCT CTTTCTCGTT GCTGCAGCCA CACGCGTTCA TAGC AGCCAG
61    TGTGTGAACC TGACCACCAG AACACAGCTG CCTCCTGCCT ACACCAACAG CTTCACCAGA
121   GGAGTCTACT ACCCAGACAA AGTCTTCAGA AGCTCTGTGC TGCACAGCAC CCAGGACCTG
181   TTCCTGCCTT TCTTCAGCAA CGTGACCTGG TTCCACGCCA TCCACGTGTC TGGCACCCAAC
241   GGCACCAAGA GATTTGACAA CCCTGTTCTT CCTTTCAATG ATGGCGTGTA CTTTGCCAGC
301   ACAGAGAAGA GCAACATCAT CCGAGGCTGG ATCTTTGGCA CCACCCTGGA CAGCAAAACC
361   CAGAGCCTGC TGATCGTGAA CAACGCCACC AACGTGGTCA TCAAGGTGTG TGAGTTCCAG
421   TTCTGCAATG ACCCTTTCCT GGGCGTGTAC TACCACAAGA ACAACAAGTC CTGGATGGAG
481   TCTGAGTTCA GAGTCTACAG CTCTGCCAAC AACTGCACAT TTGAATATGT GTCCCAGCCT
541   TTCCTGATGG ACCTGGAGGG CAAGCAGGGC AACTTTAAGA ACCTGAGAGA ATTTGTGTTC
601   AAGAACATCG ATGGCTACTT CAAGATCTAC AGCAAGCACA CACCCATCAA CCTGGTGAGA
661   GACCTGCCTC AGGGCTTCTC TGCCCTGGAG CCTCTGGTGG ACCTGCCCAT CGGCATCAAC
721   ATCACCAGAT TCCAGACCCT GCTGGCCCTG CACAGAAGCT ACCTGACCCC AGGAGACAGC
781   AGCAGCGGCT GGACAGCTGG AGCTGCTGCC TACTACGTGG GCTACCTGCA GCCCAGGACC
                                        (중략)
3421  AACACAGTTT ATGACCCTCT GCAGCCTGAG CTGGACAGCT TCAAAGAAGA GCTGGACAAG
3481  TACTTCAAGA ACCACACATC TCCAGATGTG GACCTGGGAG ACATCTCTGG CATCAATGCC
3541  TCTGTGGTGA ACATCCAGAA GGAAATTGAC AGGCTGAACG AAGTGGCCAA GAACCTGAAC
3601  GAAAGCCTCA TCGACCTGCA GGAGCTGGGC AAGTACGAGC AGTACATCAA GTGGCCTTGG
3661  TACATCTGGC TGGGCTTCAT CGCTGGCCTC ATCGCCATCG TGATGGTGAC CATCATGCTG
3721  TGCTGCATGA CCAGCTGCTG CTCTTGCCTG AAGGGCTGCT GCAGCTGTGG CAGCTGCTGC
3781  AAGTTTGATG AAGATGACTC TGAGCCTGTG CTGAAGGGCG TGAAGCTGCA CTACACA
```

✓ **[0510] SEQUENCE LISTING**

1. **SARS**-CoV-2 Consensus Spike Antigen aminoacid insert sequence of **pGX9501 (SEQ ID NO: 1)** (IgE leader sequence underlined)
2. DNA insert sequence of pGX9501 **(SEQ ID NO: 2)** (IgE leader sequence underlined)
3. Single strand DNA sequence of pGX9501 **(SEQ ID NO: 3)**
4. **SARS**-CoV-2 Outlier Spike Antigen amino acid insert sequence of **pGX9503 (SEQ ID NO 4)** (IgE leader sequence underlined)
5. DNA insert sequence of pGX9503 **(SEQ ID NO: 5)** (IgE leader sequence underlined)
6. Single strand DNA sequence of pGX9503 **(SEQ ID NO: 6)**

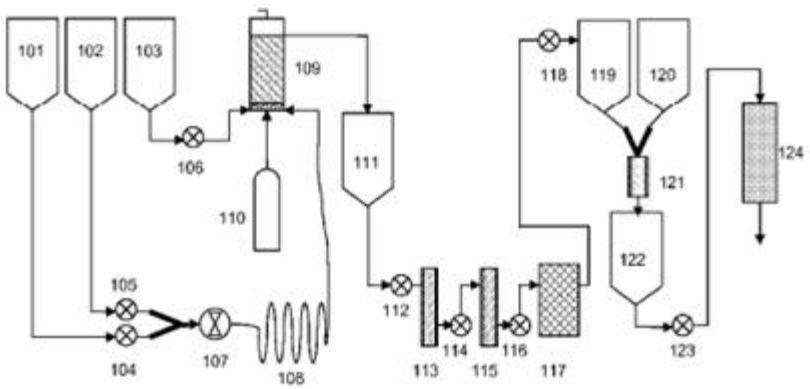
6. WO2008-148010 A1

서지사항

발명의 명칭	COMPOSITIONS COMPRISING HIGH CONCENTRATION OF BIOLOGICALLY ACTIVE MOLECULES AND PROCESSES FOR PREPARING THE SAME		현재상태	공개	
출원번호 (출원일)	PCT-US2008-064726 (2008.05.23) (우: 2007.05.23)	등록•공개번호 (등록•공개일)	WO2008-148010 A1 (2008.12.04)		
출 원 인	VGX PHARMACEUTICALS, INC.(US)	패밀리 특허	US 2건 | KR 1건 | JP 1건 | EP 1건 | CN 2건		
발명자	DRAGHIA-AKLI, Ruxandra(US) HEBEL, Henry(US) CAI, Ying(US)	공정분류	Cell lysis, Separation, Purification	세부 기술	고농도 플라스미드 DNA 제조 공정

상세사항

요약	Large scale processes for producing high purity samples of biologically active molecules of interest from bacterial cells are disclosed. The methods comprise the steps of producing a lysate solution by contacting a cell suspension of said plurality of cells with lysis solution; neutralizing said lysate solution with a neutralizing solution to produce a dispersion that comprises neutralized lysate solution and debris; filtering the dispersion through at least one filter; performing ion exchange separation on said neutralized lysate solution to produce an ion exchange eluate; and performing hydrophobic interaction separation on said ion exchange eluate to produce a hydrophobic interaction solution. Further, provided are compositions comprising large scale amounts of plasmid DNA produced by the disclosed large scale processes
청구항1 (대표 청구항)	A **large scale process for producing high purity samples** of at least one biologically active molecule of interest from **bacterial cells,** comprising the steps of: a) **producing a lysate solution** by contacting a cell suspension of said plurality of cells with **lysis solution;** b) **neutralizing** said lysate solution with a neutralizing solution to produce a dispersion that comprises neutralized lysate solution and debris; c) **filtering** the dispersion through at least one filter; d) performing ion **exchange** separation on said **neutralized** lysate solution to produce an **ion exchange eluate**; and e) performing **hydrophobic interaction** separation on said **ion exchange** eluate to produce a hydrophobic interaction solution.

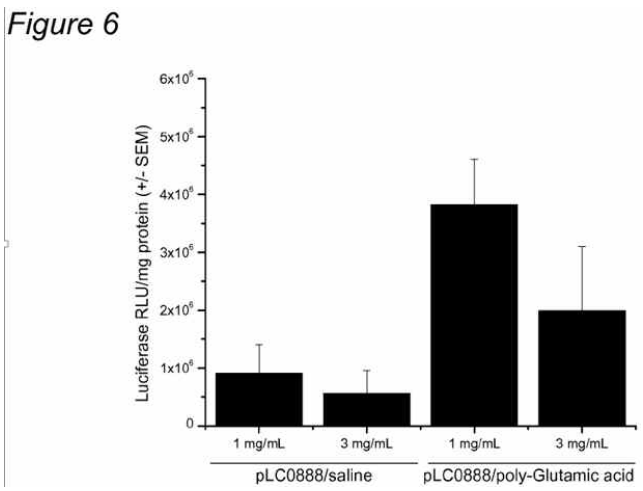
청구항2 (종속항)	The method of claim 1, wherein step a) comprises **mixing** said cell suspension with lysis solution in a **high shear, in-line mixer.**
청구항3 (종속항)	The method of claim 1 or 2, wherein step b) comprises **mixing** said lysate solution with said neutralizing solution in a **bubble mixer.**
분석내용	• 본 발명은 고농도 플라스미드 DNA를 다량으로 제조하는 방법으로, 용해 단계, 중화단계, 여과단계, ion exchange 단계, 소수성 상호 용액을 생성하는 단계로 이뤄짐 • 특히, 용해 용액과 혼합 시 고전단 혼합기와, 버블 믹서를 사용하여 혼합이 보다 잘 되도록 하고 알칼리와 플라스미드의 접촉시간을 줄여줘 플라스미드의 손상을 방지하여, 고농도의 플라스미드 DNA를 다량으로 제조하게 함 Figure 1  101: Cell resuspension tank 102: Lysis solution tank 103: NP solution tank 104: Pump for cell resuspension 105: Pump for lysis solution 106: Pump for NP solution 107: In-line mixer 108: Holding coil 109: Bubble column mixer 110: Compressed gas tank 111: Container for crude lysate 112: Pump for primary filtration 113: Primary filter 114: Pump for secondary filtration 115: Secondary filter 116: Pump for third filter (optional) 117: Third filter (optional) 118: Pump for clarified lysate 119: Container for clarified lysate 120: Water tank 121: Mixer 122: Container for diluted lysate 123: Pump for Mustang Q 124: Mustang Q cartridge **<도1> 연속 흐름(또는 유동) 공정에서 박테리아 세포로부터 DNA 플라스미드를 분리 및 정제하는 모식도**

7. US 7491537 B2

서지사항

발명의 명칭	Nucleic acid formulations for gene delivery and methods of use		현재상태	만료	
출원번호 (출원일)	US 11/561847 (2006.11.20.) (우: 2000.03.03)	등록•공개번호 (등록•공개일)	US 7491537 B2 (2009.02.17)		
출 원 인	출원인: Genetronics Biomedical Corporation(US) 현재 권리자: INOVIO PHARMACEUTICALS, INC(US)	패밀리 특허	US 5건| WO 3건| JP 3건 | EP 3건 | CN 1건 | 기타11건		
발명자	Jason G Fewell (US) Fiona MacLaughlin (US) Louis C Smith (US)	공정분류	Formulation (전달효율 향상)	세부 기술	poly glutamic acid

상세사항

요약	A nucleic acid formulation for use in gene delivery comprising a nucleic acid and an anionic polymer is disclosed. Examples of the anionic polymer includes anionic amino acid polymer or poly-amino acid (such as poly-L-glutamic acid, poly-D-glutamic acid, poly-L-aspartic acid, poly-D-aspartic acid), poly-acrylic acid, polynucleotides, poly galacturonic acid, and poly vinyl sulfate. 
청구항1 (대표 청구항)	A method of delivering a nucleic acid encoding a therapeutic gene product to a cell comprising: introducing the nucleic acid encoding the therapeutic gene product to a cell in a formulation comprising the nucleic acid formulated with an anionic polymer selected from the group consisting of: poly glutamic acid, poly aspartic acid, poly galacturonic acid, poly vinyl sulfate, and co-polymers of glutamic and aspartic acid, and salts thereof, wherein the anionic polymer is non-encapsulating and the formulation does not include a cationic polymer.

청구항2 (종속항)	The method of claim 1, wherein the anionic polymer is selected from the group consisting of **poly glutamic acid** and **poly aspartic acid**, and **salts** thereof.
분석내용	• **폴리글루탐산 제제로 구성된 유전자 전달 제제에** 관한 것으로, **본 발명자들은 폴리글루탐산 제제는 생체내에서 전기천공 보조하여, 형질감염을 증가시키는데 유용함을 확인함** • 음이온성 아미노산 중합체인 폴리글루탐산은 형질감염 효율을 증가시켜, 적은 양의 DNA가 사용될 수 있으며, 생분해성으로 독성 또는 부작용이 최소화 될 수 있음 • **폴리-L-글루타민산의 나트륨 염의 수용액**을 최대 **10mM의 정제된 플라스미드 DNA의 스톡 용액과 조합**하여, 폴리-L-글루탐산과 DNA가 결합된 후, 5M NaCl의 스톡 용액을 첨가하여 150mM NaCl의 최종 농도로 조정하여 제조함 • 제제 제조방법 [0090] Preparation of Formulations Formulations were made by aliquoting appropriate volumes of sterile stock solutions of water, plasmid, polymer, buffer and/or 5M NaCl to obtain a final plasmid in an isotonic solution. The total plasmid concentration of all formulations was measured by UV absorption at 260 nm. The osmotic pressure of selected formulations was measured using a Fiske One-Ten Micro-Sample Osmometer (Fiske Associates; Norwood, Mass.). The percentage of supercoiled plasmid was measured using 1% agarose gel electrophoresis followed by fluorimaging. Plasmids were formulated in 5-10 mM Tris, pH 7.5 or saline (150 mM NaCl) or mixed with a polymer in isotonic saline. Plasmid used for injection was formulated with various polymers in an isotonic saline solution. Typically, the concentration of plasmid was 1-2 mg/ml in saline, or formulated with polyvinylpyrrolidone (PVP, 5%) or 6 mg/ml poly-L-glutamate (Sigma, St Louis, Mo.) in saline. Anionic polymers included poly-L-glutamic acid (p-L-Glu), sodium salt, of various molecular weights (degree of polymerization (DP) of 9 (Sigma P1943), degree of polymerization of 10 (Sigma P1818),2-15 kDa (Sigma P4636),15-50 kDa (Sigma P4761) and 50-100 kDa (Sigma P4886)), poly-D-glutamic acids (p-D-Glu) of 15-50 (Sigma P4033) and 50-100 kDa (Sigma 4637), poly-L-aspartic acid (p-L-Asp), sodium salt, of 2-15 (Sigma P5387) and 15-50 kDa (Sigma P6762) and poly-acrylic acid (pAA), sodium salt, of 5 and 60 kDa. The polyamino acids were purchased from Sigma (St. Louis, Mo.), while the poly(acrylic acid) was acquired from Fluka (Switzerland). The DNA/anionic polymer formulations were preferably prepared by aliquoting appropriate volumes of sterile stock solutions of plasmid, anionic polymer and 5M NaCl to obtain selected final plasmid and anionic polymer concentrations. The anionic polymer was added to the DNA solution prior to adding salt for tonicity adjustment. Thus, poly-L-glutamate formulations are preferably prepared by combining an aqueous stock solution of sodium poly-L-glutamate (sodium salt of poly-L-glutamic acid) with a stock solution of purified plasmid DNA in saline or up to 10 mM Tris, pH 7.5. After the poly-L-glutamic acid and DNA are combined, the solution is adjusted to a final concentration of 150 mM NaCl by addition of a stock solution of 5M NaCl. The osmolality of each formulation was measured using a Fiske One-Ten Micro-Sample Osmometer (Fiske Associate, Norwood Mass.). Formulations were also characterized by measuring the optimal density at 260 and 280 nm, and by determining plasmid conformation on a 1% agarose gel.

8. WO2009-065121 A1

서지사항

발명의 명칭	INCREASED STABILITY OF A DNA FORMULATION BY INCLUDING POLY-L-GLUTAMATE		현재상태	공개	
출원번호 (출원일)	PCT-US2008-083785 (2008.11.17) (우: 2007.11.16)	등록•공개번호 (등록•공개일)	WO2009-065121 A1 (2009.05.22)		
출 원 인	VGX PHARMACEUTICALS, INC.(US)	패밀리 특허	US 2건 | WO 1건 | KR 1건 | EP 1건 | CN 1건		
발명자	DRAGHIA-AKLI, Ruxandra(US) POPE, Melissa(US)	공정분류	Formulation (전달효율 향상)	세부 기술	poly glutamic acid

상세사항

요약	Aspects of the present invention is related to DNA vaccine formulations having enhanced stability comprising at least one DNA plasmid capable of expressing an antigen in cells of mammal and poly-L-glutamate; wherein the DNA plasmid is present in the vaccine formulation at a concentration of at least 1 mg/ml, and the poly-L-glutamate is present in the amount of weight that is 1 % of the amount of DNA plasmid. Some aspects of the present invention is related to methods of stabilizing DNA plasmid in a DNA vaccine formulation. Additionally, the present invention is related to methods for introducing a DNA vaccine formulation having enhanced stability into a cell of a selected tissue in a recipient.
청구항1 (대표 청구항)	A DNA vaccine formulation having **enhanced stability** comprising at least one **DNA plasmid** capable of expressing an antigen **in cells of mammal** and poly-L-glutamate; wherein the DNA plasmid is present in the **vaccine formulation** at a concentration of at least 1 mg/ml, and the **poly-L-glutamate is present in the amount of weight that is 1% of the amount of DNA plasmid.**
청구항 2 (종속항)	The DNA vaccine formulation of claim 1 wherein the vaccine formulation is stable at room temperature for at least 24 hours.
청구항 3 (종속항)	The DNA vaccine formulation of any one of claims 1-2, wherein the vaccine formulation is **stable** at **4 ℃ for at least 24 hours.**
분석내용	• 폴리-L-글루타메이트를 포함시킴으로써 **안정성이 증가된 DNA 플라스미드 백신 제형으로, 폴리-L-글루타메이트가 DNA 플라스미드 양의 1%의 중량으로 존재함** • 상기 백신 제형의 DNA 플라스미드가 **실온에서 2일, 4 ℃에서 90일 이상** 동안 **안정함을 확인함** (도 7,8,9,10)

9. US 6752781 B2

서지사항

발명의 명칭	Durable hypodermic jet injector apparatus and method		현재상태	소멸	
출원번호 (출원일)	US 10/057052 (2002.01.25.) (우: 2001.06.08.)	등록•공개번호 (등록•공개일)	US 6752781 B2 (2004.06.22)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	US 3건		
발명자	Sergio Landau(US), Daniel Williamson(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A gas-powered, durable, needle-less hypodermic jet injection device (10, 210) includes a hand-held injector (12, 212) which receives into an injection cylinder a volume of liquid medication to be injected in the form of a high velocity jet capable of penetrating the skin without the use of a hypodermic needle. The injection device provides an injection orifice, and an injection piston. Forceful movement of the injection piston causes a high velocity injection jet of liquid medication to be expelled from the injection cylinder via the injection orifice. The injection device includes features which improve its usability, particularly for users with hands that are possibly weak, feeble, or arthritic, for example; and also includes additional features which improve manufacturability, durability, and cost effectiveness of the device.
청구항1 (대표 청구항)	A gas powered hypodermic jet injection device, said device comprising: a device body having a forward end; an injection cylinder at the forward end of said device body, and said injection cylinder having a cylinder bore in which an injection piston is sealingly movable to cooperatively define a variable-volume chamber for holding a dose of liquid medication; said injection cylinder defining a fine-dimension injection orifice in liquid flow communication with said variable-volume chamber to receive and discharge liquid medication as a forceful high velocity jet upon forceful movement of said injection piston in said cylinder; a power source in said device body for forcefully moving said injection piston in said cylinder in response to communication of gas pressure to a gas pressure piston; said power source including a source of pressurized gas for selective communication with said gas pressure piston; a trigger assembly for selectively effecting communication of pressurized gas from said source to said gas pressure piston; and

a lost motion preventing mechanism selectively drivingly connecting said gas pressure piston to said injection piston;

wherein said lost motion prevention mechanism includes said gas pressure piston defining a bore, an injection ram interfacing at a forward end with said injection piston and adjacent to an aft end portion thereof being received into said bore and being selectively associated with said gas pressure piston, and said lost motion prevention mechanism in a first condition selectively allowing relative axial motion of said gas pressure piston and said injection ram, and also said lost motion prevention mechanism in a second condition selectively coupling said injection ram to said gas pressure piston for axial motion in unison therewith.

10. US 7054685 B2

서지사항

발명의 명칭	Method and apparatus for reducing electroporation-mediated muscle reaction and pain response		현재상태	소멸	
출원번호 (출원일)	US 10/215963 (2002.08.08.) (우: 1999.03.25.)	등록•공개번호 (등록•공개일)	US 7054685 B2 (2006.05.30)		
출 원 인	Genetronics, Inc.(US)	패밀리 특허	US 3건 | EP 1건 | WO 1건 | 기타 4건		
발명자	Steve Dimmer(US), Gunter Hofmann(US), Daniel Holt(US), Gurvinder Nanda(US), Edward M. Nolan(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A method for delivery of an agent to a cell using electroporation is disclosed. The method includes positioning a first electrode and a second electrode such that an electrical signal passed between the first electrode and the second electrode passes through the cell. The method also includes passing an electrical signal between the first electrode and the second electrode, the electrical signal having a frequency greater than about 10 kHz. In one embodiment of the method, the electrical signal has a bipolar waveform. In another embodiment of the method, the electrodes are positioned at a treatment site, e.g., a tumor, for in vivo delivery of an agent.
청구항1 (대표 청구항)	An electroporation system comprising: a. an electroporation therapy apparatus comprising a body and a plurality of electrodes disposed in the body; b. a connector that provides electrical communication between the electrodes disposed in the body of the electroporation therapy apparatus and an electroporation instrument; and c. an electroporation instrument that delivers a therapeutic electrical signal, wherein the therapeutic electrical signal comprises an electroporation signal and an agent movement signal.

11. US 6883222 B2

서지사항

발명의 명칭	Drug cartridge assembly and method of manufacture		현재상태	등록	
출원번호 (출원일)	US 10/272689 (2002.10.16.)	등록•공개번호 (등록•공개일)	US 6883222 B2 (2005.04.26)		
출 원 인	Bioject Inc.(US)	패밀리 특허	US 1건 | JP 1건 | EP 1건 | WO 1건 | 기타 3건		
발명자	Sergio Landau(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A method of manufacture for a drug cartridge assembly. The method includes providing a drug cartridge, providing a nozzle sub-assembly, and sterilizing the drug cartridge and nozzle sub-assembly. The method further includes assembling the drug cartridge and nozzle sub-assembly together in a configuration that enables ejection of liquid out of the drug cartridge through the nozzle sub-assembly. The method further includes filling the drug cartridge with a liquid, such as an injectable drug. The method may include separate sterilization of the drug cartridge and nozzle sub-assembly, using different sterilization processes. Portions of the method may be performed prior to sterilization within a first cleanroom, with subsequent steps being performed in a second cleanroom having a substantially lower particulate-per-volume rating than the first cleanroom.
청구항1 (대표 청구항)	A method of preparing a sterile drug cartridge assembly, comprising: providing a drug cartridge; providing a nozzle sub-assembly, where the drug cartridge and nozzle-sub-assembly are adapted to be engaged together to enable ejection of liquid from the drug cartridge out through the nozzle sub-assembly; assembling the nozzle subassembly and otherwise preparing the nozzle sub-assembly for sterilization in a first cleanroom; sterilizing the nozzle sub-assembly; sterilizing the drug cartridge; and positioning the drug cartridge in a ready-to-use position within the nozzle sub-assembly, and filling and sealing the drug cartridge, where the positioning, filling and sealing are performed within a second cleanroom, the second cleanroom having a particulate-per-volume rating which is at least ten times lower than that of the first cleanroom.

12. WO2003-059952 A1

서지사항

발명의 명칭	BISPECIFIC ANTIBODY DNA CONSTRUCTS FOR INTRAMUSCULAR ADMINISTRATION		현재상태	공개	
출원번호 (출원일)	PCT-IB2003-000098 (2003.01.16.) (우: 2002.01.18.)	등록•공개번호 (등록•공개일)	WO2003-059952 A1 (2003.07.24)		
출 원 인	INOVIO AS(NO)	패밀리 특허	KR 1건 | JP 1건 | CN 1건 | US 1건 | EP 1건 | WO 1건 | 기타 3건		
발명자	BOGEN, Bjarne(NO), MATHIESEN, Iacob(NO), TJELLE, Torunn, Elisabeth(NO)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A multi-chain protein can be produced in a subject by intramuscular injection of one or more vectors that code for the chains of the protein and, optionally, by applying one or more electrical pulses across the injection site. A preferred multi-chain protein is an immunoglobulin. This approach to antibody production has various applications, including for expressing multi-chain proteins in vivo for disease therapy and for eliciting an immune response to one or more foreign antigenic determinants of the expressed protein.
청구항1 (대표 청구항)	Use of at least one expression vector in the preparation of a pharmaceutical composition for use in production of a protein, wherein said at least one vector (i) encodes a protein that comprises at least two different polypeptide chains and, when injected into muscle of a subject, (ii) results in production of the polypeptide chains and secretion of the protein.

13. WO2003-076006 A2 (EP 1480720 B1)

서지사항

발명의 명칭	ELECTRODE ASSEMBLY FOR CONSTANT-CURRENT ELECTROPORATION AND USE		현재상태	공개	
출원번호 (출원일)	PCT-US2003-006833 (2003.03.06.) (우: 2002.03.07)	등록•공개번호 (등록•공개일)	WO2003-076006 A2 (2003.09.18)		
출 원 인	ADVISYS, INC.(US)	패밀리 특허	EP 1건 | 기타 10건		
발명자	WESTERSTEN, Allan(US) DRAGHIA-AKLI, Ruxandra(US) CARPENTER, Robert, H.(US) 외 2명	공정분류	전달체	세부 기술	5 전극 배열

상세사항

요약	The present invention relates to a modular electrode system, and its use, for facilitating the introduction of a macromolecule into cells of a selected tissue in a body or plant. The modular electrode system comprises a plurality of needle electrodes; a hypodermic needle; an electrical connector that provides a conductive link from a programmable constant-current pulse controller to the plurality of needle electrodes; and a power source. In a preferred embodiment of the present invention, an operator can grasp the plurality of needle electrodes that are mounted on a support structure and firmly insert them into the selected tissue in a body or plant. The macromolecules are then delivered via the hypodermic needle into the selected tissue. The programmable constant-current pulse controller is activated and constant-current electrical pulse is applied to the plurality of needle electrodes. The applied constant-current electrical pulse facilitates the introduction of the macromolecule into the cell between the plurality of electrodes. Cell death due to overheating of cells is minimized by limiting the power dissipation in the tissue by virtue of constant current pulses.
청구항 1 (대표 청구항)	A **modular electrode system** for facilitating the introduction of a macromolecule into a cell of a selected tissue in a **body** or **plant**, comprising: (a) a plurality of needle electrodes for penetrating the selected tissue, the plurality of needle electrodes being mounted on a support structure and arranged in a spaced relationship, and (b) a constant-current pulse generator subsystem in electrical communication with the plurality of needle electrodes for applying a constant-current pulse between any plurality of electrodes.
분석내용	• 본 발명은 신체 또는 식물 조직의 **세포 내로 핵산분자의 도입을 용이**하게 하기 위한 **모듈형 전극 시스템**에 관한 것임 • 정전류 펄스 컨트롤러가 활성화되고 정전류 전기 펄스가 복수의 바늘 전극에 인가되면, 전극 사이의 셀으로 고분자의 도입을 용이하게 함 • 5 전극배열을 사용하여 **전기천공 중첩 지점이 발생하지 않는 분산 패턴을 생성할 수 있어 과열로 인한 셀의 사멸 및 조직에 손실을 제한함**

14. WO2004-004825 A2

서지사항

발명의 명칭	ELECTROPORATION DEVICE AND INJECTION APPARATUS		현재상태	공개	
출원번호 (출원일)	PCT-GB2003-002887 (2003.07.04) (우: 2002.07.04)	등록•공개번호 (등록•공개일)	WO2004-004825 A2 (2004.01.15)		
출 원 인	INOVIO AS(NO)	패밀리 특허	US 5건 | JP 2건 | EP 1건 | CN 1건 | 기타 15건		
발명자	MATHIESEN, Iacob(NO) TJELLE, Torunn, Elisabeth(NO) REKDAHL, Knut, Arvid, Sørensen(NO)	공정분류	전달체	세부 기술	전기 천공 장치와 인젝션 장치

상세사항

요약	An apparatus is provided for injecting a fluid into body tissue, the apparatus comprising: a hollow needle (6); and fluid delivery means (12, 10), wherein the apparatus is adapted to actuate the fluid delivery means (12, 10) in use so as to automatically inject fluid into body tissue during insertion of the needle into the said body tissue.
청구항1 (대표 청구항)	**Apparatus for injecting a fluid into body tissue**, the apparatus **comprising**: a **hollow needle**; and **fluid delivery means**, wherein the apparatus is adapted to actuate the fluid delivery means in use so as to concurrently inject fluid into body tissue during insertion of the needle into the said body tissue.
청구항 2 (종속항)	Appatatus as claimed in claim 1 adapted <u>to automatically inject fluid into body tissue during insertion</u>.
청구항 4 (종속항)	Apparatus as claimed in any of claims 1 to 3 , further comprising means for **sensing** when the **needle** has been inserted to a **sufficient depth for injection of the fluid to commence**.
청구항 6 (종속항)	Apparatus as claimed in claim 4, wherein the **sensing** means comprises an **ultrasound probe.**
분석내용	• 본 발명은 **hollow needle**과 **유체 공급 수단**으로 구성된 **전기천공 전달 장치**에 관한 것임 • 전기천공법은 DNA가 근육 내에 주입되고서 **근다발간 또는 근육 세포 사이의 지방조직에 갇힐 가능성**이 있어 <u>DNA의 균일 분포가 어려움</u>. 또한 많은 양의 유체를 주입하면 환자에게 상당한 <u>통증</u>을 유발하는 문제가 있음 • 본 발명은 <u>DNA가 주입되는 것과 동시에, 주입된 직후 근육이 전기적으로 자극됨으로써, 세포막에 DNA가 통과할 수 있는 크기의 미세 구멍이 생성되어 DNA가 전달됨</u> • <u>바늘이 삽입되는 동안 유체를 점진적으로 주입할 수 있어 신체 조직에서 유체가보다 균일하게 분포하는 이점이 있음</u>

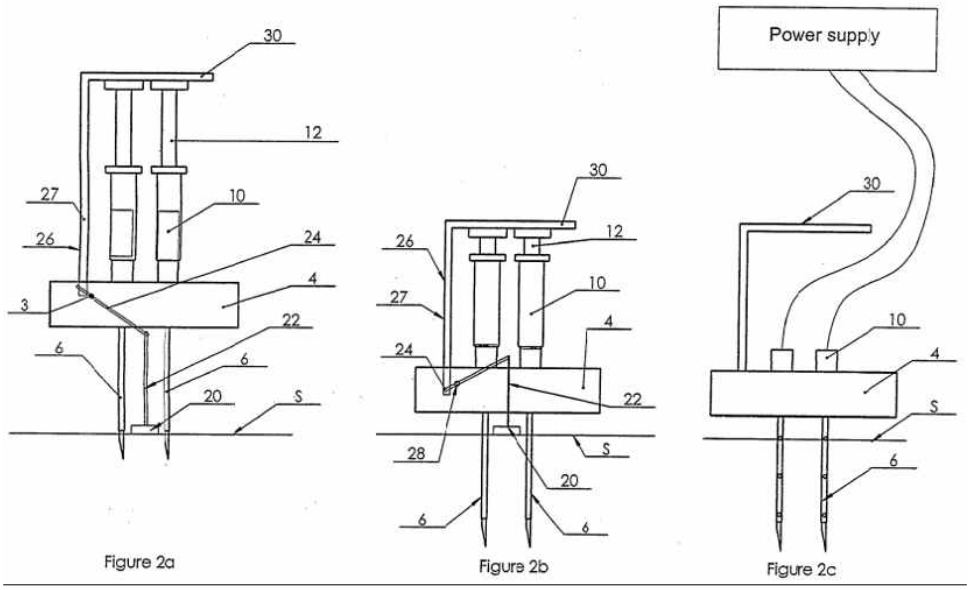

30
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Figure 2a
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Figure 2b
Power supply
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6
Figure 2c

15. US 7717874 B2					
서지사항					
발명의 명칭	Needle-free injection system		현재상태	등록	
출원번호 (출원일)	US 10/857591 (2004.05.28)	등록•공개번호 (등록•공개일)	US 7717874 B2 (2010.05.18)		
출 원 인	Bioject, Inc.(US)	패밀리 특허	JP 2건 | US 2건 | EP 2건 | WO 1건 | 기타 2건		
발명자	Sergio Landau(US), Ryan R. Beylund(US), James M. Bonicatto(US), Keith K. Daellenbach(US), Robert A. Miller(US), Theodore Walaka Sedler(US), John L. Staylor(US)	공정분류	전달체	세부 기술	전기천공 관련 기술
상세사항					
요약	A needle-free injection device in which a gas cartridge or other source of pressurized gas is used to advance a piston and forcibly expel injectable fluid out through an injection orifice. When a gas cartridge is used, the gas cartridge may be moveable from an initial position to an actuating position in which gas is released to drive the injection, and a recoil inhibiter may be employed to prevent the gas cartridge from moving back to the initial position. A gas cartridge seal may be disposed on the gas cartridge and moveable with the gas cartridge to seal the gas cartridge against an interior wall of a gas cartridge housing. The needle-free injection device may also be configured so that sealing is compromised upon full advancement of the piston, so as to de-pressurize the device after delivery of an injection.				
청구항1 (대표 청구항)	A needle-free injection device, comprising: a piston configured to be advanced during delivery of an injection; a gas cartridge disposed within a gas cartridge housing and movable relative to the gas cartridge housing from an initial position to an actuating position, in which a pierceable sealed opening at a forward end of the gas cartridge is pierced by a piercing member to enable pressurized gas to be released from the gas cartridge to act upon a rearward end of the piston, thereby driving the piston forward to forcibly expel injectable fluid out through an injection orifice; and a recoil inhibiter configured to constrain movement of the gas cartridge after delivery of the injection so that the gas cartridge is movable from the initial position to the actuating position during delivery of the injection, but is prevented from moving from the actuating position back to the initial position after delivery of the injection is complete; wherein the recoil inhibitor includes a ratchet structure that is formed in an elongate slot, and where a pawl device includes a resilient leg that ratchets against an edge of the elongate slot as the pawl device is moved forward relative to the gas cartridge housing.				

16. US 7442182 B2

서지사항

발명의 명칭	Spring powered needle-free injection system		현재상태	등록	
출원번호 (출원일)	US 10/974004 (2004.10.25.) (우: 2003.10.24.)	등록•공개번호 (등록•공개일)	US 7442182 B2 (2008.10.28)		
출 원 인	Bioject, Inc.(US)	패밀리 특허	US 1건 | WO 1건		
발명자	Sergio Landau(US), Christopher Sautter(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A needle-free injection device, including a plunger and a spring operatively coupled with the plunger. The plunger is slidably disposed within a fluid chamber, is retractable to draw injectable fluid into the fluid chamber through an injection orifice, and may be advanced within the fluid chamber to forcibly eject injection fluid out through the injection orifice. The spring is configured to be compressed during arming of the injection device, and decompressed during discharge to forcibly advance the plunger within the fluid chamber. The injection device further includes an actuator operable to cause the spring to be compressed during arming of the injection device, and selectively operable prior to decompression of the spring to cause the plunger to be moved to a desired position within the fluid chamber.
청구항1 (대표 청구항)	A needle-free injection device, comprising: a housing; an elongate shaft; a first spring stop member; a second spring stop member, where one of the first and second spring stop members is threadably engaged with a threaded portion of the shaft; a spring disposed between the first and second spring stop members; and a plunger secured to the second spring stop member and slidably disposed within a fluid chamber, the plunger being operable to be retracted to draw injectable fluid into the fluid chamber through an injection orifice, and advanced within the fluid chamber to cause the injectable fluid to be forcibly ejected out through the injection orifice, where the injection device is configured so that, when the injection device is in an unarmed condition, and upon rotation of the shaft in a first direction, the first and second spring stop members are brought closer together to compress the spring, where the injection device includes a latching mechanism configured to latch the first and second spring stop members together upon full compression of the spring, so as

to maintain the spring in a fully compressed state between the first and second spring stop members,

where the latching mechanism includes a latch member that is pivotally connected to one of the first and second spring stop member and configured to move through the housing when the one of the first and second spring stop member moves through the housing, and

where, when the first and second spring stop members are latched together, the first and second spring stop members are configured for movement through the housing while maintaining the spring in a fully compressed state.

17. US 7922709 B2

서지사항

발명의 명칭	Enhanced delivery of naked DNA to skin by non-invasive in vivo electroporation		현재상태	소멸	
출원번호 (출원일)	US 11/291459 (2005.11.30.) (우: 1998.07.13.)	등록•공개번호 (등록•공개일)	US 7922709 B2 (2011.04.12)		
출 원 인	Genetronics, Inc.(US)	패밀리 특허	JP 1건 | US 7건 | EP 3건 | WO 1건 | 기타 2건		
발명자	Lei Zhang(US), Dietmar P. Rabussay(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	In vivo methods are provided for using an electric field to delivery therapeutic or immunizing treatment to a subject by applying non-invasive, user-friendly electrodes to the surface of the skin. Thus, therapeutic or immunizing agents can be delivered into cells of skin for local and systemic treatments or for immunization with optimal gene expression and minimal tissue damage. In particular, therapeutic agents include naked or formulated nucleic acid, polypeptides and chemotherapeutic agents.
청구항1 (대표 청구항)	A method for delivering an isolated polynucleotide species that encodes a therapeutic gene product into skin cells of a subject, comprising: a) introducing about 0.05 μg to about 100 μg of at least one isolated polynucleotide species encoding a therapeutic gene product into each of one or more skin tissue sites of a subject; and b) substantially contemporaneously with the introduction of the isolated polynucleotide species, applying one or more electric pulses across at least two noninvasive electrodes to generate a total charge transfer of about one mC to about 1000 mC per skin tissue site so as to allow the polynucleotide species to enter cells within the skin tissue site, thereby delivering the isolated polynucleotide species into skin cells of the subject.

18. US 7664545 B2

서지사항

발명의 명칭	Electrode assembly for constant-current electroporation and use		현재상태	등록	
출원번호 (출원일)	US 11/495021 (2006.07.28.) (우: 2002.03.07)	등록•공개번호 (등록•공개일)	US7664545 B2 (2010.02.16)		
출 원 인	출원인: VGX Pharmaceuticals(US) 현재권리자: INOVIO PHARMACEUTICALS(US)	패밀리 특허	WO 1건 | US 2건 | EP 1건 | 기타 6건		
발명자	Allan Westersten(US) William R. Wilkinson(US) RuxandraDraghia-Akli(US)	공정분류	전달체	세부기술	핀전극 배열을 가진 정전류 시스템

상세사항

요약

The present invention relates to a modular electrode system, and its use, for facilitating the introduction of a macromolecule into cells of a selected tissue in a body or plant. The modular electrode system comprises a non-symmetrically arranged plurality of needle electrodes; a hypodermic needle; an electrical connector that provides a conductive link from a programmable constant-current pulse controller to the plurality of needle electrodes; and a power source. In a preferred embodiment of the present invention, an operator can grasp the plurality of needle electrodes that are mounted on a support structure and firmly insert the them into the selected tissue in a body or plant. The macromolecules are then delivered via the hypodermic needle into the selected tissue. The programmable constant-current pulse controller is activated and constant-current electrical pulse is applied to the plurality of needle electrodes. The applied constant-current electrical pulse facilitates the introduction of the macromolecule into the cell between the plurality of electrodes. Cell death due to overheating of cells is minimized by limiting the power dissipation in the tissue by virtue of constant-current pulses.

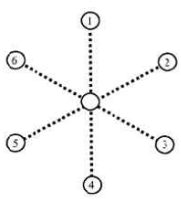


Figure 1

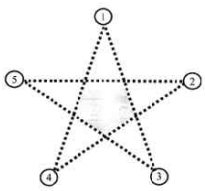
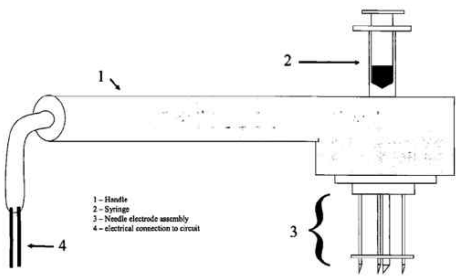


Figure 2



청구항1 (대표 청구항)	A **modular electrode system** for introducing of a macromolecule into a **muscle tissue** in a body, comprising: a plurality of **needle electrodes** for penetrating the muscle tissue, the plurality of **needle electrodes** being mounted on a support structure and arranged non-symmetrically around a **centerpoint**, and a constant-current pulse generator subsystem in electrical communication with the plurality of needle electrodes, wherein the constant-current pulse generator subsystem is capable of applying a decentralized **constant-current pulse between any plurality of electrodes and the plurality of needle electrodes are constructed from a material that will make galvanic contact with the tissues**; and a programmable constant-current pulse controller having an impedance meter in electrical communication with the plurality of needle electrodes and the constant-current pulse generator subsystem, wherein the programmable constant-current pulse controller is capable of maintaining a constant current independent of any resistance change in the muscle tissue during the decentralized constant-current pulse.
분석내용	• **본 발명의 핀전극 배열을 가진 정전류 시스템**은 전극 **내 도관에 충돌하는 이온 플럭스를 정밀하게 제어**하고 **전력 손실이 감소**되고, 열 발생을 감소시켜 **조직손상을 줄여줌** • 본 발명의 전극 배열은 **기존 6 전극배열**(도 1)과 달리 **5 전극배열** (도 2)을 사용하여, 전기 천공 동안 해당 영역에서 **중첩 지점이 발생하지 않아 분산 패턴을 생성할 수 있어 조직 손상을 줄여줌**

19. US 7547293 B2					
서지사항					
발명의 명칭	Triggering mechanism for needle-free injector		현재상태	등록	
출원번호 (출원일)	US 11/539585 (2006.10.06)	등록•공개번호 (등록•공개일)	US 7547293 B2 (2009.06.16)		
출 원 인	Bioject, Inc.(US)	패밀리 특허	US 2건 | EP 1건 | WO 1건		
발명자	Daniel E. Williamson(US), Ryan R. Beylund(US)	공정분류	전달체	세부 기술	전기천공 관련 기술
상세사항					
요약	Needle-free hypodermic jet injection devices having an actuation system to effect an injection from a drug delivery system. The actuation system includes an injection force assembly adapted to transmit a driving force to the drug delivery system. The actuation system further includes a trigger assembly adapted to alter the actuation system between a plurality of configurations including a fired configuration in which the injection force assembly transmits a driving force to the drug delivery system. In some embodiments, the device has a recoil restriction system including a restriction member adapted to couple the recoil restriction system to the trigger assembly and a recoil member coupled to the injection force assembly and movable relative to the restriction member. The restriction member limits movement of the recoil member once the recoil member moves a predetermined distance relative to the restriction member.				
청구항1 (대표 청구항)	A needle-free injection device comprising: a drug delivery system including a nozzle having a drug chamber and an outlet orifice, the drug delivery system adapted to expel a volume of liquid from the drug chamber through the outlet orifice; an actuation system including: an injection force assembly adapted to transmit a driving force to the drug delivery system; and a trigger assembly adapted to alter the actuation system between a plurality of configurations including a fired configuration in which the injection force assembly transmits a driving force to the drug delivery system; and a recoil restriction system including a restriction member adapted to couple the recoil restriction system to the trigger assembly, and a recoil member coupled to the injection force assembly and movable relative to the restriction member, wherein the restriction member limits movement of the recoil member once the recoil member moves a predetermined distance relative to the restriction member.				

20. US 10369359 B2

서지사항

발명의 명칭	Device and method for single-needle in vivo electroporation		현재상태	등록	
출원번호 (출원일)	US 11/704591 (2007.02.09.) (우: 2006.02.11.)	등록•공개번호 (등록•공개일)	US 10369359 B2 (2019.08.06)		
출 원 인	Genetronics, Inc.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 1건 | US 4건 | EP 2건 | WO 2건 | 기타 9건		
발명자	Rune Kjeken(US), Iacob Mathiesen(US), Elisabeth Torunn Tjelle(US), George McHugh(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	Described is a device and method for administration of molecules to tissue in vivo for various medical applications, the device comprising a single hypodermic injection needle and at least two spaced elongate electrodes which provide for the ability, when the needle is inserted into tissue, such as skin or muscle, to pulse tissue with a non-uniform electric field sufficient to cause reversible poration of cells lying along or in close proximity to the track made by the needle upon its insertion into said tissue.
청구항1 (대표 청구항)	A device for electroporation of tissue in vivo for delivering therapeutic substances into cells of a tissue comprising: a single electroporating needle having a tissue-piercing tip, said needle comprising: a shaft that is elongated, hollow, and adapted for delivery of a fluid comprising a therapeutic substance to said tissue, said shaft having a length running from one end of the needle to the tip of the needle at an other end of the needle, and at least two electrodes exposed along an outer surface of said shaft that are adapted to produce a generally cylindrical electric field, said at least two electrodes spaced and electrically isolated from one another and situated spiraling and parallel to one another along the length of said shaft; an electrical energy source; and electric conduits capable of connecting each of said at least two electrodes to the electrical energy source, wherein when said shaft is inserted into said tissue and said at least two electrodes are energized by said electrical energy source, said at least two electrodes are in contact with said tissue and are capable of generating the generally cylindrical electric field in a treatment zone surrounding the length of said shaft, wherein the at least two electrodes are configured to transmit electric pulses from the electrical energy source that have a current in a range of 1 mAmp to 400 mAmp so as to cause cells in said treatment zone to become reversibly porated so as to allow said cells to take up said therapeutic substance.

21. US 7942845 B2

서지사항

발명의 명칭	Needle-free injector and process for providing serial injections		현재상태	등록	
출원번호 (출원일)	US 11/765245 (2007.06.19.) (우: 2006.09.19.)	등록•공개번호 (등록•공개일)	US 7942845 B2 (2011.05.17)		
출 원 인	Bioject, Inc.(US)	패밀리 특허	US 1건 | EP 1건 | WO 1건		
발명자	Daniel E. Williamson(US), Ryan R. Beylund(US), Keith K. Daellenbach(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	Needle-free injection devices having a drive assembly to provide an operative force to effect an injection and a dosing assembly to prepare the device for a subsequent injection. In some embodiments, the dosing assembly is configured to transfer injectate from an injectate source to the injectate assembly. In some embodiments, a portion of energy available to the drive assembly urges the injectate towards the injectate assembly. In some embodiments, the device includes a nozzle assembly having one or more ports.
청구항1 (대표 청구항)	A needle-free injection device for delivering serial injections comprising: a body configured to house a plurality of systems; a delivery system adapted to deliver an injection, the delivery system comprising: an injectate assembly adapted to eject a volume of injectate responsive to application of an operative force to the injectate assembly, the injectate assembly having a nozzle assembly including a chamber and one or more ports, each terminating in an outlet orifice, the nozzle assembly further including a plunger selectively movable within the chamber; a drive assembly adapted to provide the operative force to move the plunger using energy from an energy supply; and a dosing assembly configured to transfer injectate from an injectate source to the injectate assembly, wherein a portion of energy available to the drive assembly urges injectate from the injectate source to the injectate assembly; and an actuation system adapted to actuate the delivery system for delivery of an injection, the actuation system comprising: a trigger assembly configured to restrict selectively operation of the drive assembly.

22. WO2008-048632 A1					
서지사항					
발명의 명칭	ELECTROPORATION DEVICES AND METHODS OF USING SAME FOR ELECTROPORATION OF CELLS IN MAMMALS		현재상태	공개	
출원번호 (출원일)	PCT-US2007-022139 (2007.10.17)	등록•공개번호 (등록•공개일)	WO2008-048632 A1 (2008.04.24)		
출 원 인	VGX PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 2건 | US 1건 | EP 3건 | WO 1건 | 기타 10건		
발명자	BROWN, Patricia, A.(US), DRAGHIA-AKLI, Ruxandra(US), KHAN, Amir, S.(US), POPE, Melissa, A.(US)	공정분류	전달체	세부 기술	전기천공 관련 기술
상세사항					
요약	Aspects of the present invention relate to electroporation devices and methods of using same to effectively facilitate the introduction of a biomolecule into cells of a selected tissue in a body, in particular skin such as intradermic or subcutaneous tissue. In some aspects, the present invention is a skin EP device, which produces a pulse of energy and delivers same to the skin tissue using a skin electrode array and maintains a constant current in the same skin tissue based on user input, including a preset current, and allows the storage and acquisition of current waveform data.				
청구항1 (대표 청구항)	An electroporation device configured to deliver to a desired tissue of a mammal a pulse of energy producing a constant current similar to a preset current input by a user, the electroporation device comprising: an electroporation component capable of delivering the pulse of energy that produces the constant current in the desired tissue, the electroporation component having a feedback mechanism; a skin electrode assembly including an electrode array having a plurality of skin electrodes in a spatial arrangement, wherein the skin electrode assembly receives the pulse of energy from the electroporation component and delivers same to the desired tissue through the skin electrodes; wherein at least one of the plurality of skin electrodes is neutral during delivery of the pulse of energy and measures impedance in the desired tissue and communicates said impedance to the electroporation component; and wherein the feedback mechanism can receive the measured impedance and can adjust the pulse of energy delivered by the electroporation component to maintain the constant current.				

23. US 7931640 B2

서지사항

발명의 명칭	Method for muscle delivery of drugs, nucleic acids and other compounds		현재상태	소멸	
출원번호 (출원일)	US 12/070233 (2008.02.15.) (우: 1997.04.03.)	등록•공개번호 (등록•공개일)	US 7931640 B2 (2011.04.26)		
출 원 인	Inovio AS(US)	패밀리 특허	KR 1건 | JP 2건 | CN 1건 | US 7건 | EP 2건 | WO 2건 | 기타 11건		
발명자	Iacob Mathiesen(NO), Terje Lomo(NO)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A method is disclosed for delivering molecules such as pharmaceutical drugs and nucleic acids into skeletal muscle in vivo. The molecule is first injected into the muscle at one or multiple sites. Immediately or shortly after injection, electrodes are placed flanking the injection site and a specific amount of electrical current is passed through the muscle. The electrical current makes the muscle permeable, thus allowing the molecule to enter the cell. In the case where nucleic acid is injected, the efficiency of transfer permits expression of protein encoded by the nucleic acid in an amount that exhibits systemic biological activity and which generates a robust immune response.
청구항1 (대표 청구항)	A method of immunizing a mammal, comprising: a. administering to a muscle tissue of a mammal a first composition comprising a protein or peptide antigen; b. following administration of the antigen, delivering to the muscle tissue an electroporative electric stimulus; and c. following delivery of the electroporative electric stimulus, administering to the muscle tissue of the mammal a second composition comprising an expression vector that directs the expression of a polynucleotide that encodes the antigen, wherein performance of the method immunizes the mammal against the antigen.

24. WO2009-045813 A1					
서지사항					
발명의 명칭	MATERIALS AND METHODS FOR THE DELIVERY OF BIOMOLECULES TO CELLS OF AN ORGAN		현재상태	공개	
출원번호 (출원일)	PCT-US2008-077499 (2008.09.24.) (우: 2007.10.01.)	등록•공개번호 (등록•공개일)	WO2009-045813 A1 (2009.04.09)		
출 원 인	VGX PHARMACEUTICALS, INC.(US)	패밀리 특허	US 1건 | WO 1		
발명자	DRAGHIA-AKLI, Ruxandra(US)	공정분류	전달체	세부 기술	전기천공 관련 기술
상세사항					
요약	The present invention is directed towards materials and methods of delivering biomolecules to cells that define an organ, the organ being in situ, and electroporating cells defining the organ by delivering to the cells an amount of energy effective to electroporate the cells. The present invention is also directed towards materials and methods of expressing heterologous polypeptides in organs of a subject and electroporating cells defining the organ by delivering to the cells an amount of energy effective to electroporate the cells.				
청구항1 (대표 청구항)	A method of delivering a biomolecule to a cell that defines an organ, the organ being in situ, comprising: delivering the biomolecule to the organ, and providing an amount of energy to the organ effective to electroporate the cells that define the organ.				

25. US 8617099 B2

서지사항

발명의 명칭	Injection device plunger auto-disable		현재상태	등록	
출원번호 (출원일)	US 12/627605 (2009.11.30.) (우: 2007.11.26.)	등록•공개번호 (등록•공개일)	US 8617099 B2 (2013.12.31)		
출 원 인	Bioject Inc.(US)	패밀리 특허	JP 1건 | CN 2건 | US 3건 | EP 2건 | WO 2건 | 기타 4건		
발명자	Daniel E. Williamson(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A nozzle assembly for a needle-free injection device. The nozzle assembly includes a nozzle body including an injectate chamber and one or more outlet orifices and a plunger configured to move through the injectate chamber toward the one or more outlet orifices. In some embodiments, the plunger includes a first portion and a second portion removably joined by a frangible region. In some embodiments, the plunger includes extensions configured to couple the plunger to a drive assembly of a needle-free injection device.
청구항1 (대표 청구항)	A nozzle assembly for a needle-free injection device comprising: a nozzle body including an injectate chamber and an outlet orifice; and a plunger configured to move through the injectate chamber toward the outlet orifice, the plunger including a proximal portion, a distal portion and frangible region along which the proximal portion and distal portion are configured to uncouple upon injection; wherein the proximal portion is adapted to rotate relative to and away from the distal portion about a longitudinal axis of the plunger upon injection, the rotation being sufficient to prevent the proximal region from catching on the distal portion when the distal portion is withdrawn; wherein the proximal portion remains in the injectate chamber upon retraction of the distal portion from the injectate chamber.

26. WO2010-121160 A1

서지사항

발명의 명칭	CONTACTLESS ELECTROPERMEABILIZATION ELECTRODE AND METHOD		현재상태	공개	
출원번호 (출원일)	PCT-US2010-031431 (2010.04.16.) (우: 2009.04.16.)	등록•공개번호 (등록•공개일)	WO2010-121160 A1 (2010.10.21)		
출 원 인	VGX PHARMACEUTICALS, LLC(US)	패밀리 특허	KR 4건 | US 2건 | EP 1건 | WO 1건 | 기타 1건		
발명자	KARDOS, Thomas Joseph(US), KEMMERRER, Stephen Vincent(US), KJEKEN, Rune(US), BRODERICK, Kate(US), MCCOY, Jay(US), FONS, Michael P.(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	Devices and methods for delivering an electropermeabilizing pulse of electric energy to a tissue surface to enable delivery into cells in the tissue therapeutic substances. The device incorporates a source capable of generating a sufficient voltage potential to deliver a spark across a gap and delivers same to the tissue surface.
청구항1 (대표 청구항)	A method of enabling the delivery of therapeutic substances into cells of tissue of a mammal by using a spark electropermeabilizing device to deliver an electropermeabilizing electric voltage potential to the surface of a mammalian tissue, comprising: generating a voltage potential sufficient to jump a gap of predetermined distance; delivering said generated voltage potential in the form of a spark that can jump said gap to the surface of the mammalian tissue without causing macroscopic damage to an integrity of the surface of the mammalian tissue; and delivering the therapeutic substances to cells within the mammalian tissue.

27. US 10045911 B2

서지사항

발명의 명칭	Intradermal injection device		현재상태	등록	
출원번호 (출원일)	US 12/824114 (2010.06.25)	등록•공개번호 (등록•공개일)	US 10045911 B2 (2018.08.14)		
출 원 인	Genetronics, Inc.(US)	패밀리 특허	US 3건 | EP 1건 | CN 1건 | WO 1건 | 기타 1건		
발명자	Daniel E. Williamson(US), John R. Marshall(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	Embodiments herein relate to the field of injections, for instance needle-free injections, and more specifically, to methods and apparatus for spring-driven intramuscular and intradermal injections. Provided in some embodiments are needle-free injectors adapted to deliver intradermal injections, as well as vial adaptors that are adapted to function as spacers when used with a needle-free injection device.
청구항1 (대표 청구항)	A needle-free injection device comprising: a body terminating in a nozzle; a fluid reservoir housed within the body, the fluid reservoir being adapted to receive a fluid injectate; a plunger disposed within the fluid reservoir; a shaft to which the plunger is mounted such that when the shaft is driven forward, the plunger is responsively driven forward; a spring-driven propulsion system having a first spring adapted to apply a bias force to the shaft and thus to the plunger to cause ejection of the fluid injectate through the nozzle; a lever adapted to arm the spring-driven propulsion system; and a rod extending between the lever and the shaft, the rod configured to transmit a load force between the lever and the shaft via a body of the rod so as to load the first spring, wherein the load force is opposite the bias force.

28. US 10610684 B2

서지사항

발명의 명칭	Variable current density single needle electroporation system and method		현재상태	등록	
출원번호 (출원일)	US 12/836163 (2010.07.14.) (우: 2008.01.17.)	등록•공개번호 (등록•공개일)	US 10610684 B2 (2020.04.07)		
출 원 인	Genetronics, Inc.(US)	패밀리 특허	KR 1건 | JP 2건 | CN 1건 | US 2건 | EP 2건 | WO 1건 | 기타 7건		
발명자	Rune Kjeken(NO), Stephen Vincent Kemmerrer(US), Feng Lin(US), Dietmar Rabussay(US), Thomas Joseph Kardos(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	This invention comprises an improved electroporation electrode system comprising a single needle and a ring or donut shaped electrode wherein the difference in surface area of the electrodes provide for a substantial reduction of current density near the surface of the treated tissue and a more concentrated current density sufficient for electroporation only in tissues adjacent to the terminal portion of the single needle electrode. Thus, this invention provides for targeting specific tissue for electroporation and also should provide for lessening the sensation of electric current in the treated tissue.
청구항1 (대표 청구항)	An electroporation system for delivering a molecule into cells of a focused area of tissue by providing a differential current density to a mammal, the electroporation system comprising: a) a geometric planar ring electrode with a multiplicity of electrically conductive projections thereon, wherein said geometric planar ring electrode is electrically isolatable into two electrically conductive halves; b) a tissue-piercing elongate electrode having a proximal and a distal end, said tissue-piercing elongate electrode having a nonconductive portion and a conductive portion, said nonconductive portion lying between said proximal end and between about 2.5 cm and at least 0.1 cm from the distal end, said nonconductive portion comprising either an insulator coating on said tissue-piercing elongate electrode or a nonconductive material; c) a housing associated with said geometric planar ring electrode and tissue-piercing

elongate electrode;

d) a charging unit for charging a capacitor; and

e) a computer in electrical communication with said charging unit, said computer comprising software capable of performing programming functions for said system;

f) wherein the tissue-piercing elongate electrode defines a plurality of apertures that are positioned on the conductive portion of the tissue piercing-elongate electrode such that there are between approximately 10 and approximately 100 apertures per centimeter of length of the conductive portion, and the apertures are spaced around an entire circumference of the conductive portion and have a diameter in a range of 30 microns to 80 microns, wherein the aperture positioning, spacing, and diameters are configured to provide even distribution of an injection fluid over an entire length of the conductive portion.

29. WO2011-109399 A1

서지사항

발명의 명칭	MULTIPLE TISSUE LAYER ELECTROPORATION APPLICATOR AND DEVICE		현재상태	공개	
출원번호 (출원일)	PCT-US2011-026688 (2011.03.01.) (우: 2010.03.01.)	등록•공개번호 (등록•공개일)	WO2011-109399 A1 (2011.09.09)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | US 2건 | EP 1건 | WO 1건 | 기타 3		
발명자	BRODERICK, Kate(US), LIN, Feng(US), MCCOY, Jay(US), KEMMERER, Stephen V(US), KJEKEN, Rune(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	The present invention relates to dual depth electroporation devices capable of electorporating both muscle tissue and skin tissue in a single application in order to generate a broad immune response in a subject, and uses of the same.
청구항1 (대표 청구항)	A dual depth electroporation device capable of electorporating both muscle tissue and skin tissue in a single application, comprising: a electrical pulse generator; an array in electrical communication with said electrical pulse generator, said array having a first set of needle electrodes and a second set of electrodes; wherein the first set of needle electrodes is for intramuscular delivery of a first electrical pulse, the first set of needle electrodes having a length of about 10mm to about 35mm, and the second set of electrodes is for intradermal delivery of a second electrical pulse, the second set of needle electrodes having a length of about 0.01mm to about 4mm.

30. WO2011-109406 A1

서지사항

발명의 명칭	A TOLERABLE AND MINIMALLY INVASIVE SKIN ELECTROPORATION DEVICE		현재상태	공개	
출원번호 (출원일)	PCT-US2011-026701 (2011.03.01.) (우: 2010.03.01.)	등록•공개번호 (등록•공개일)	WO2011-109406 A1 (2011.09.09)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 1건 | US 1건 | EP 1건 | WO 1건 | 기타 11건		
발명자	BRODERICK, Kate(US), MCCOY, Jay(US), KEMMERRER, Stephen V(US), LIN, Feng(US), KJEKEN, Rune(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A novel electroporation device for the delivery of vaccines that is both effective in generating a protective immune response and tolerable delivery to a subject (or near painless); and also methods of using same device to vaccinate a subject against a variety of infectious diseases and types of cancer in a near painless.
청구항1 (대표 청구항)	What is claimed is: 1. An electroporation device capable of delivering to a subject a tolerable electrical potential to layers of epidermal tissue between stratum corneum and basal layers that results in electroporation of cells in said tissue comprising: a voltage generator; and an array having a plurality of electrodes in electrical communication with the voltage generator; wherein each one of the plurality of electrodes are spaced apart from each adjacent electrode at a distance of about 0.5 mm to about 2.5 mm; the voltage generator delivers via the electrodes an electrical potential of about 0.1 volts to about 50 volts to the epidermal tissue; and the electrodes have a tip on the distal end that is blunt with a sharp point allowing the electrode to penetrate layers of epidermis tissue between stratum corneum and basal layers, and delivers the electrical potential from the voltage generator to the epidermis tissue.

31. WO2011-137221 A1

서지사항

발명의 명칭	ORAL MUCOSAL ELECTROPORATION DEVICE AND USE THEREOF		현재상태	공개	
출원번호 (출원일)	PCT-US2011-034277 (2011.04.28.) (우: 2010.04.28)	등록•공개번호 (등록•공개일)	WO2011-137221 A1 (2011.11.03)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 4건 | CN 1건 | US 3건 | EP 1건 | WO 1건 | 기타 2건		
발명자	KEMMERRER, Stephen V.(US), MCCOY, Jay(US), BRODERICK, Kate(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	The present invention relates to oral electroporation (EP) devices that are able to generate an electroporation causing electrical field at the mucosal layer, and preferably in a tolerable manner. Further, it includes the generation of a protective immune response, cellular and/or humoral, using the oral EP device along with a genetic construct that encodes an immunogenic sequence.
청구항1 (대표 청구항)	A device for electroporating cells of a mucosal membrane of a mammal, wherein the device comprises: an electrode microneedle plate, a counter electrode plate, a main housing in physical communication with said microneedle plate and counter electrode plate, wherein the main house is in fluid communication with a syringe capable of storing a pharmaceutical formulation for delivery, and an energy source in electrical communication with said microneedle plate and capable of generating an electric potential and delivering said electric potential to said cells through said microneedle plate.

32. WO2013-066427 A1

서지사항

발명의 명칭	A MINIMINALLY INVASIVE DERMAL ELECTROPORATION DEVICE		현재상태	공개	
출원번호 (출원일)	PCT-US2012-044539 (2012.06.28.) (우: 2011.06.28.)	등록•공개번호 (등록•공개일)	WO2013-066427 A1 (2013.05.10)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 4건 | JP 5건 | CN 1건 | US 3건 | EP 3건 | WO 1건 | 기타 9건		
발명자	BRODERICK, Kate(US), KEMMERRER, Stephen(US), MCCOY, Jay(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	The disclosure is directed to a device for electroporating and delivering one or more antigens and a method of electroporating and delivering one or more antigens to cells of epidermal tissues using the device. The device comprises a housing, a plurality of electrode arrays projecting from the housing, each electrode array including at least one electrode, a pulse generator electrically coupled to the electrodes, a programmable microcontroller electrically coupled to the pulse generator, and an electrical power source coupled to the pulse generator and the microcontroller. The electrode arrays define spatially separate sites.
청구항1 (대표 청구항)	A device for electroporating and delivering one or more antigens, the device comprising: a housing; a plurality of electrode arrays projecting from the housing, the electrode arrays defining spatially separate sites, each electrode array including at least one electrode; a pulse generator electrically coupled to the electrodes; a programmable microcontroller electrically coupled to the pulse generator; and an electrical power source coupled to the pulse generator and the microcontroller, wherein the electrodes are configured to deliver an electroporating pulse to cells of epidermal tissues, and wherein the microcontroller is configured to adjust parameters of the electroporating pulse of each electrode array independently.

33. WO2013-019603 A2

서지사항

발명의 명칭	LINEAR EXPRESSION CASSETTES AND USES THEREOF		현재상태	공개	
출원번호 (출원일)	PCT-US2012-048494 (2012.07.27.) (우: 2011.07.29.)	등록•공개번호 (등록•공개일)	WO2013-019603 A2 (2013.02.07)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	US 1건 | WO 1건		
발명자	BRODERICK, Kate(US), SARDESAI, Niranjan(US), LIN, Feng(US), SHEH, Xuefei(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	Provided herein are linear nucleic expression cassettes and methods of using same in a non-invasive method of vaccination. The method combines electroporation and linear DNA constructs encoding antigens to elicit antigen-specific immune responses.
청구항1 (대표 청구항)	A nucelic acid construct capable of expressing a desired antigen in cells of a subject, comprising: a linear expression cassette comprising an antigen encoding sequence selected from the group consisting of SEQ ID Os: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 38, 44, 46, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, and sequences that are at least 98% similar thereof; or antigen encoding sequence encoding an antigen selected from the group consisting of SEQ ID NOs: 1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 39-43, 45, 47, 48-193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, and 249, and sequences that are at least 98% similar thereof.

34. WO2017-112898 A1

서지사항

발명의 명칭	ELECTROPORATION DEVICE HAVING A BATTERY PACK WITH POWER SWITCH		현재상태	공개	
출원번호 (출원일)	PCT-US2016-068413 (2016.12.22.) (우: 2015.12.22.)	등록•공개번호 (등록•공개일)	WO2017-112898 A1 (2017.06.29)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 1건 | US 1건 | EP 1건 | WO 1건 | 기타 8건		
발명자	STADELMANN, Beat(US), KEMMERRER, Stephen(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	An electroporation device having a battery pack including a plurality of battery cells and at least one lead in electrical communication with a circuit board. The battery pack including a safety switch and a controller for selectively placing the battery cells in electrical communication with the one lead. Where the controller is in operable communication with the safety switch such that when the controller detects one or more operating conditions the controller instructs the safety switch to electrically isolate the lead from the battery cells. The battery pack also includes a manual switch, and where activation of the switch causes the controller to instruct the safety switch to electrically isolate the lead from the battery cells.
청구항1 (대표 청구항)	A handset of an electroporation device, the handset comprising: a housing defining a volume therein; a circuit board at least partially positioned within the volume; an electrode extending from the housing and in electrical communication with the circuit board; and a battery pack including: a battery pack housing, a plurality of battery cells positioned within the battery pack housing, a first power lead in electrical communication with the circuit board, a second power lead coupled to the plurality of battery cells and in electrical communication with the circuit board, a safety switch positioned within the battery pack housing and coupled between the first power lead and the plurality of battery cells, wherein the safety switch is adjustable between an ON state, where the plurality of battery cells are in electrical communication with the first power lead, and an OFF state, where the plurality of battery cells are not in electrical communication with the first power lead.

35. WO2017-117251 A1

서지사항

발명의 명칭	ELECTROPORATION DEVICE WITH IMPROVED SIGNAL GENERATOR		현재상태	공개	
출원번호 (출원일)	PCT-US2016-068940 (2016.12.28.) (우: 2015.12.28.)	등록•공개번호 (등록•공개일)	WO2017-117251 A1 (2017.07.06)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 1건 | US 1건 | EP 1건 | WO 1건 | 기타 8건		
발명자	STADELMANN, Beat(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A handset for an electroporation device having an improved signal generator. The signal generator includes a primary winding and a plurality of secondary windings where the plurality of secondary windings are coupled together in a series configuration. A storage capacitor and the fly-back diode are coupled to each of the plurality of secondary windings. The signal generator includes a signal amplifier, and a power switch. The power switch is configured to supply a voltage from a power source across the primary winding.
청구항1 (대표 청구항)	A handset for use in an electroporation device, the handset comprising: a housing; a signal amplifier positioned within the housing, the signal amplifier including: a primary winding, a plurality of secondary windings coupled together in a series configuration, wherein a storage capacitor and a fly-back diode are coupled to each of the plurality of secondary windings; and an array having a plurality of electrodes in electrical communication with the signal amplifier.

36. WO2017-117273 A1

서지사항

발명의 명칭	INTRADERMAL JET INJECTION ELECTROPORATION DEVICE		현재상태	공개	
출원번호 (출원일)	PCT-US2016-068972 (2016.12.28.) (우: 2015.12.28.)	등록•공개번호 (등록•공개일)	WO2017-117273 A1 (2017.07.06)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 2건 | US 2건 | EP 1건 | WO 1건 | 기타 3건		
발명자	MCCOY, Jay(US), BRODERICK, Kate(US), KEMMERRER, Stephen(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	An jet injection and electroporation device for use with an agent cartridge defining a volume containing a pre-measured dose of agent therein, the electroporation device including a housing having an axis extend therethrough, a nozzle at least partially positioned within the housing, and a cavity sized to receive at least a portion of the agent cartridge therein. The device also includes an array having a plurality of electrodes extending therefrom, a propulsion cartridge configured to operatively engage the cartridge when the agent cartridge is positioned within the cavity; and a power supply in electrical communication with the array.
청구항1 (대표 청구항)	An electroporation device for use with an agent cartridge defining a volume containing a pre-measured dose of agent therein, the electroporation device comprising: a housing having an axis extend therethrough; a nozzle at least partially positioned within the housing; a cavity sized to receive at least a portion of the agent cartridge therein, and wherein the nozzle is in fluid communication with the volume of the agent cartridge when the agent cartridge is positioned within the cavity; an array having a plurality of electrodes extending therefrom; a propulsion cartridge configured to operatively engage the agent cartridge when the agent cartridge is positioned within the cavity; and a power supply in electrical communication with the array.

37. WO2017-117508 A1

서지사항

발명의 명칭	ELECTROPORATION DEVICE WITH DETACHABLE NEEDLE ARRAY WITH LOCK-OUT SYSTEM		현재상태	공개	
출원번호 (출원일)	PCT-US2016-069438 (2016.12.30.) (우: 2015.12.30.)	등록•공개번호 (등록•공개일)	WO2017-117508 A1 (2017.07.06)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 1건 | JP 1건 | CN 1건 | US 2건 | EP 2건 | WO 1건 | 기타 13건		
발명자	STADELMANN, Beat(US), KEMMERRER, Stephen(US), CAMPILLO-AGUSTI, Alejandro(US), HO, Eduardo, E.(US), LOVELL, Nathan(US), MASTERSON, Steven(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	An electroporation device with a needle array removably attached thereto, the needle array having a body, a shroud movable with respect to the body between a rest position and one or more actuated positions, and an auto-lock assembly. Where the auto-lock assembly is adjustable between a locked configuration, where the shroud is not movable with respect to the body, and an unlocked configuration, where the shroud is movable with respect to the body, and where biasing the shroud from the rest position to the one or more actuated positions and back to the rest position adjusts the auto-lock from the unlocked configuration to the locked configuration.
청구항1 (대표 청구항)	An electroporation device comprising: a handset, the handset including: a housing defining a mounting point, and a signal generator positioned within the housing; and a needle array removably couplable to the mounting point and in electrical communication with the signal generator when the needle array is coupled to the mounting point, the needle array including: a body, a shroud movable with respect to the body between a rest position and one or more actuated positions, an auto-lock adjustable between a locked configuration, where the shroud is not movable with respect to the body, and an unlocked configuration, where the shroud is movable with respect to the body, and wherein biasing the shroud from the rest position to the one or more actuated positions and back to the rest position adjusts the auto-lock from the unlocked configuration to the locked configuration.

38. US 2020-0016400 A1

서지사항

발명의 명칭	METHOD AND DEVICE FOR MINIMALLY INVASIVE IN VIVO TRANSFECTION OF ADIPOSE TISSUE USING ELECTROPORATION		현재상태	공개	
출원번호 (출원일)	US 16/335444 (2017.09.22.) (우: 2016.09.23.)	등록•공개번호 (등록•공개일)	US 2020-0016400 A1 (2020.01.16.)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	KR 2건 | JP 1건 | CN 1건 | US 1건 | EP 1건 | WO 1건 | 기타 7건		
발명자	Paul FISHER(US), Kate BRODERICK(US), Jay MCCOY(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A method and device for electroporating adipocytes in the adipose layer of tissue, where the device includes a frame, a first electrode coupled to the frame having a first contact surface, a second electrode coupled to the frame having a second contact surface, and where the first contact surf ace and the second contact surface define a treatment zone therebetween. The method including positioning a fold of tissue between the first and second electrodes such that the treatment zone formed between the two electrodes includes an adipose layer of tissue and no skeletal muscle.
청구항1 (대표 청구항)	A method of electroporating adipocytes in the adipose layer of tissue, the method comprising providing a first electrode having a first contact surface, and wherein the first contact surface has a first perimeter; providing a second electrode having a second contact surface, and wherein the second contact surf ace has a second perimeter; obtaining a fold of tissue; positioning the fold of tissue between the first electrode and the second electrode such that the first contact surface of the first electrode is facing toward the second contact surface of the second electrode, producing a treatment zone therebetween, and wherein the tissue positioned within the treatment zone includes an adipose layer of tissue; and applying an electrical signal to the first electrode and second electrode.

39. WO2021-189012 A1

서지사항

발명의 명칭	VACUUM-ASSISTED ELECTROPORATION DEVICES, AND RELATED SYSTEMS AND METHODS		현재상태	공개	
출원번호 (출원일)	PCT-US2021-023344 (2021.03.19.) (우: 2020.03.20.)	등록•공개번호 (등록•공개일)	WO2021-189012 A1 (2021.09.23)		
출 원 인	INOVIO PHARMACEUTICALS, INC.(US)	패밀리 특허	US 1건 | WO 1건		
발명자	FISHER, Paul(US), KEMME, Andrea(US), SCHADE, Eric(US), MCCOY, Jay(US), BRODERICK, Kate(US), GENEROTTI, Alison A.(US)	공정분류	전달체	세부 기술	전기천공 관련 기술

상세사항

요약	A device for vacuum-assisted in vivo electroporation of tissue includes a housing that defines a chamber and at least one opening into the chamber. A port extends through the housing, is remote from the at least one opening, and is connectable to a vacuum source. The port is configured to communicate vacuum pressure from the vacuum source to the chamber. A plurality of electrodes are positioned within the chamber and are configured to deliver one or more electroporation pulses to a targeted portion of tissue extending through the opening and held in the chamber responsive to the vacuum pressure.
청구항1 (대표 청구항)	A device for vacuum-assisted in vivo electroporation of tissue, comprising: a housing defining a chamber and at least one opening into the chamber; at least one port extending through the housing, wherein the at least one port is remote from the at least one opening and is connectable to a vacuum source, such that the at least one port is configured to communicate vacuum pressure from the vacuum source to the chamber; and a plurality of electrodes positioned within the chamber, wherein the plurality of electrodes are configured to deliver one or more electroporation pulses to a targeted portion of tissue extending through the at least one opening and at least momentarily held in the chamber responsive to the vacuum pressure.

3. 소결

- DNA 백신은 항원 염기서열을 가진 DNA(플라스미드)를 체내 주입 후 전기천공(electroporation) 등의 방법으로 세포 내로 보내고 이후 우리 몸의 세포가 항원 단백질을 생산하게 하여 면역원성을 가지게 하는 백신임
- 코로나 19 관련 DNA 백신은 현재 상용화한 백신은 존재하지 않는 것으로 파악되었음
- 2021.7.19. 일자기준 임상 3상인 기업은 Zydus Cadila, INOVIO가 있고, 국내기업으로는 제넥신, 진원생명과학이 DNA 백신을 개발 중인 것으로 알려져 있음
- 코로나19 DNA 백신 관련 기술은 항원설계 기술 2건이 있는 것으로 파악되었으며, 항원설계 기술은 Zydus Cadila가 1건(WO2021-214703), INOVIO가 1건(WO2021-173829) 보유한 것으로 나타났음
- 코로나19 DNA 백신에 대한 것은 아니나 추후에 적용가능한 기술로는 INOVIO가 백터설계 기술 1건, 세포용해 기술 1건, 정제기술 1건, 제형기술 2건, 전달체 31건을 보유하고 있는 것으로 파악되었음
- 코로나19 DNA 백신에서는 발현벡터를 사용해야 하고, 선도기업 중 발현벡터로 Zydus Cadila는 pVAX1를 사용하고, INOVIO는 pGX0001을 사용한 것으로 파악되었음
- 따라서, 추후 코로나19 DNA 백신 개발 시 상기 발현벡터로 pVAX1, pGX0001를 요소기술로 사용할 수 있음. 따라서 pVAX1, pGX0001에 대한 특허가 존재하여 특허권의 독점적인 효력이 미칠 수 있으므로 이에 대한 확인이 필요한 것으로 사료됨

Ⅳ. 코로나19 DNA 백신의 자유기술의 영역

○ 특허발명 중에는 신규성 또는 진보성이 없어서 원래 특허권이 부여되지 말아야 하는 경우에는 특허를 무효로 함으로써 공익이 침해받지 않게 보호하여야 함

○ 부당하게 부여된 특허권에 대한 문제를 바로잡는 방식은 국가마다 절차에 차이가 있기는 하나 침해로 피소된 자가 특허권 침해소송 절차 중에 특허의 무효를 주장한 경우라면, 침해 판단이전에 특허가 유효한 것인지 판단하는 것에 상당한 자원[14]의 투입이 요구됨.

○ 따라서 자유실시기술의 법리는 침해분쟁의 소송에서 침해로 피소된 자가 부당하게 수여된 특허의 권리 범위로부터 벗어날 수 있도록 특허의 무효처리 절차를 가로질러 지름길의 역할을 하는 것임

○ 이러한 자유실시기술의 법리[15]는 권리범위확인심판을 청구하거나 특허권 침해의 소를 제기한 경우 "확인대상발명(침해로 피소된 피고 실시기술)이 특허발명의 권리범위에 속하는지를 판단함에 있어서 특허발명과 대비되는 발명(침해로 피소된 실시기술)은 공지의 기술만으로 이루어지거나 그 기술분야에서 통상의 지식을 가진 자가 공지기술로부터 용이하게 발명할 수

14) 김관식, '특허권의 문언침해와 자유실시기술의 항변의 허부', 사법발전재단 사법41호, 2017. 353면("특허무효심판이 제기되면, 특허권자는 이에 대응하여 자신의 특허의 무효사유를 해소하기 위해 정정청구 혹은 특허무효심판이 계속 중이 아니라면 별도의 정정심판을 청구하는 것이 가능하고, 정정이 허용되면 적법한 정정의 효력은 특허 출원 시로 소급하므로, 정정이 확정되면 특허무효심판은 소급적으로 정정된 청구항을 대상으로 처음부터 다시 그 절차를 진행하게 된다. 그결과 절차가 과도하게 지연되어 소송경제에 반할 우려가 있다.").

15) 정차호, "권리범위확인심판 및 침해소송에서의 공지기술의 항변 및 자유실시기술의 항변", 성균관법학 제27권 제3호, 2015. 275~277면 각주 10, 16, 23("중국에서는 현유기술(現有技術, existing technology), 대만에서는 현존기술(現存技術)이라고 부르며, 어떤 논문에서는 공지기술의 항변을 "existing technology defense"라고 칭하며, 자유실시기술의 법리는 독일 학설인 '자유로운 기술수준의 항변(Einrede desfreiden Standes der Technik)'에서 유래되어 일본의 일부 판결에서 수용된 것으로 통상 '자유실시기술의 항변(공지기술의 항변)'이라고 하는데 공지기술의 항변은 신규성 영역을 판단하는 데 사용되고 자유실시기술의 항변은 진보성도 판단한다는 점에서 두 항변은 구별된다."), 또한, 최근 대법원 2017. 11. 14. 선고 2016후366판결 및 특허법원 2016.11.24. 선고 2016허2096 판결과 2016. 1. 15. 선고 2015허4019 판결에서 이것을 '자유실시기술의 법리'라고 칭하고 있어서, 이 논문에서는 '자유실시기술의 법리'로 용어를 통일하여 지칭하는 것으로 한다.

있는 경우에는 특허발명과 대비할 필요 없이 특허발명의 권리범위에 속하지 아니한다."는 법리임[16)]

- 또한, 자유실시기술의 법리는 실질적으로 무권리(Nichtecht)임에도 형식상 유효한 권리로 취급되는 오인특허의 권리행사를 저지하는 대항권(Gegenrecht)의 개념으로 독일에서 발전되어 나온 것으로서, 독일 연방대법원(BHG) 1986년 Formstein 사건에서 이러한 유형의 법리를 일정 조건하에 인정하면서 받아들여지게 되었음[17)]

- 우리나라에서는 다수의 대법원 판례에서 이러한 자유실시기술의 법리를 침해소송과 권리범위확인심판에서 인정하고 있음

- 추후 코로나19 DNA 백신 개발 시 발현벡터로 pVAX1, pGX0001 기술을 이용하는 경우에 대한 침해 분쟁을 미연에 방지하고자 자유실시기술 영역에 해당되는지 여부에 대해서 살펴봄

16) 대법원 2007. 5. 11. 선고 2007후654 판결; 2008. 7. 10. 선고 2008후64 판결
17)조영선, 특허법 제5판, 박영사, 2015, 492면

VECTOR

구분	원천(인용)문헌	내용
pVAX1	INVITROGEN: "pVAX1 (Catalog no. V260-20) 25-0256" INVITROGEN HOMEPAGE (WWW.INVITROGEN.COM), [Online] <URL:https://tools.thermofisher.com/content/sfs/manuals/pvax1_man.pdf> [revision date 2 March 2012] EP 1117421 B1 (출 1999.10.05. 소멸)	[INIVITROGEN - 1 page] pVAX1™ is a 3.0 kb plasmid vector designed for use in the development of DNA vaccines. The vector was constructed to be consistent with the Food and Drug Administration (FDA) document, "Points to Consider on Plasmid DNA Vaccines for Preventive Infectious Disease Indications", published December 22, 1996 (see FDA "Points to Consider" below). Features of the vector allow high-copy number replication in E. coli and high-level transient expression of the protein of interest in most mammalian cells. ... pVAX1™ was constructed by modifying the vector, pcDNA™3.1, to accommodate the following considerations put forth by the FDA Center for Biologics Evaluation and Research (CBER) in its document, "Points to Consider on Plasmid DNA Vaccines for Preventive Infectious Diseases Indications" (Docket no. 96N-0400). ▶ pVAX1의 vendor인 introgen에서 발행한 pVAX1에 대한 매뉴얼로, pVAX1은 pcDNA3.1을 modify한 벡터이며, 1996년 발행된 FDA 문서에 준하여 제작되었음을 개시함. 특허에서는 EP 1117421 B1(1999.10.05. 출원) 문헌에서 DNA vaccination vector 중 하나로 pVAX1을 사용하고 있어 pVAX1 vector의 개발 시기는 1996~99년 사이일 것으로 추정됨. 따라서 현 시점에서 *pVAX1 vector를 이용한 DNA 백신 개발 기술은 자유실시가 가능한 기술*로 판단됨
pGX0001	US 11154602 B2 (출 2018.12.13. 등록)	[발명의 설명] ... The plasmid may also be pGX001 (Inovio), which is modified from pVAX1 (Thermo Fisher Scientific, Waltham, Mass.). ...Example 4: Plasmid Construction and Structure The vector backbone is pGX0001, a 2998 bp modified pVAX1 expression vector under the control of the human cytomegalovirus immediate-early promoter (hCMV promoter). The original pVAX1 was obtained from Thermo Fisher Scientific. The pGX0001 backbone includes the kanamycin resistance gene (KanR) and plasmid origin of replication (pUC ori) for production purpose. Those elements are not functional in eukaryotic cells. The map and description of the modified expression vector pVAX1 (pGX0001) are shown in FIG. 4. Modifications were introduced into pVAX1 to create pGX0001. These modifications are listed in Table 4, and no issues have been detected regarding plasmid amplification and antigen transcription and translation. No further changes in the sequence of pGX0001 have been observed to date using pGX0001 as the backbone. Base pairs 2, 3 and 4 are

changed from ACT to CTG in backbone, upstream of CMV promoter.

TABLE 4

Modification	Base Pair	Description
C > G	241	in CMV promoter
C > T	1158	backbone, downstream of the bovine growth hormone polyadenylation signal (bGH polyA)
A > -	2092	backbone, downstream of the Kanamycin resistance gene
C > T	2493	in pUC origin of replication (pUC ori)
G > C	2969	in very end of pUC Ori upstream of RNASeH site

▶ INOVIO가 출원한 US 10130705 B2(2014.10.02. 출원)의 실시예에서 pGX0001 vector를 이용한 단백질 발현 실험 관련 내용을 최초로 개시하며, 이후 출원된 암백신 기술인 인용문헌 US 11154602 B2의 실시예에서 pGX0001 vector의 구축방법 대하여 좀 더 상세하게 개시하고 있음. INOVIO에서 자체적으로 pVAX1을 modify한 vector이며 pVAX1과 유사한 활성을 나타냄. 다만 pVAX1에서 서열 5개를 변경한 modification에 불과하며 pVAX1과 동일한 용도로 사용되므로 별도로 특허로 권리를 확보하지는 않은 것으로 예상되어 *pGX0001 vector를 이용한 DNA 백신 개발 기술은 자유실시가 가능한 기술*로 판단됨

V. 결론 및 시사점

○ DNA 백신은 이중나선형 형태로 단일가닥인 RNA보다 분자 구조상 안정적이기에 운반과 보관 측면에서 상대적으로 쉽다는 장점이 있음

○ 현재 DNA백신은 주로 말과 같은 동물 백신으로만 활용되고 있고, 인체를 대상으로 한 임상시험에서 잠재적 면역반응을 유도하지 못한 상태이며, 지카바이러스, 메르스 등 백신 개발 과정의 임상이 진행 중임

○ 021.7.19. 일자기준 임상 3상인 기업은 Zydus Cadila, INOVIO가 있고, 국내기업으로는 제넥신, 진원생명과학이 DNA 백신을 개발 중인 것으로 알려져 있음

○ 코로나19 DNA 백신 관련 기술은 항원설계 기술 2건이 있는 것으로 파악되었으며, 항원설계 기술은 Zydus Cadila가 1건(WO2021-214703), INOVIO가 1건(WO2021-173829) 보유한 것으로 나타났음

○ 코로나19 DNA 백신에 대한 것은 아니나 추후에 적용 가능한 기술로는 INOVIO가 백터설계 기술 1건, 세포용해 기술 1건, 정제기술 1건, 제형기술 2건, 전달체 31건을 보유하고 있는 것으로 파악되었으며, 제넥신은 벡터설계 기술 2건, 아쥬반트 기술 3건, 진원생명과학은 세포 용해기술 3건, 정제기술 1건, 제형기술 1건을 보유하고 있는 것으로 파악되었음

○ 코로나19 DNA 백신에서는 발현벡터를 사용해야 하고, 선도기업 중 발현벡터로 Zydus Cadila는 pVAX1를 사용하고, INOVIO는 pGX0001을 사용한 것으로 파악되어 추후 코로나19 DNA 백신 개발 시 발현벡터로 pVAX1, pGX0001 기술을 이용하는 경우에 대한 침해 분쟁을 미연에 방지하고자 자유실시기술 영역에 해당되는지 여부에 대해서 살펴보았음

- 발현벡터로 pVAX1를 이용하는 기술은 현재로부터 20년 이전에 존재한 문헌에 의하여 공지된 것으로 판단됨
- pGX0001는 pVAX1에서 서열 2개를 변경하여 개질한 기술로 US 10130705 B2(2016.08.18. 공개)에 의해 공지된 바 있고, 이에 대하여 별도의 권리로 확보하지 않은 것으로 파악됨
- 발현벡터로 pVAX1, pGX0001을 이용하는 기술은 자유기술의 영역에 해당되어 특허권의 효력이 미치지 아니할 것이어서 이를 적극적으로 활용하여 기술개발 하는 것이 필요함