Resolving the CRISPR Catch-2023: a Tale of Two Gaps

Fyodor Urnov aka Prof. Debbie ~~Downer~~ Realist

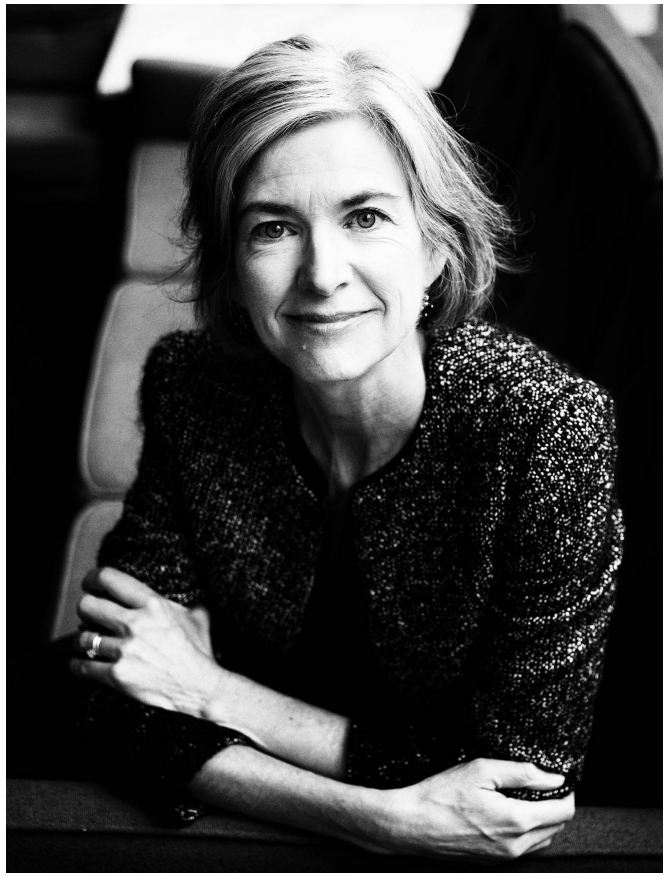
Professor of Molecular Therapeutics,
Department of Molecular and Cell Biology,
University of California, Berkeley

Scientific Director, Innovative Genomics Institute, UC Berkeley

Fyodor Urnov: disclosures

- Cimeio Therapeutics: SAB chair, paid advisor, hold equity
- Ionis Pharmaceuticals: paid advisor
- Tune Therapeutics: scientific co-founder, paid advisor, hold equity
- Vertex Pharmaceuticals: paid consultant on exa-cel program

Jennifer Doudna

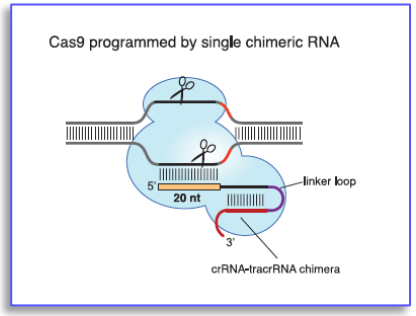


“We have a responsibility to pursue CRISPR’s enormous potential to achieve previously impossible solutions to some of the world’s big challenges — solutions that will be available to anyone.”

2012:

A Programmable Dual-RNA–Guided DNA Endonuclease in Adaptive Bacterial Immunity

Martin Jinek,[1,2]* Krzysztof Chylinski,[3,4]* Ines Fonfara,[4] Michael Hauer,[2]†
Jennifer A. Doudna,[1,2,5,6]‡ Emmanuelle Charpentier[4]‡



2023:

FDA Accepts Biologics License Applications for exagamglogene autotemcel (exa-cel) for Severe Sickle Cell Disease and Transfusion-Dependent Beta Thalassemia

June 8, 2023

- First CRISPR gene-editing filings to be accepted for review by FDA -

- FDA grants Priority Review for severe sickle cell disease (SCD) and Standard Review for transfusion-dependent beta thalassemia (TDT) –

- PDUFA target action date of December 8, 2023, for SCD and March 30, 2024, for TDT –

editas MEDICINE

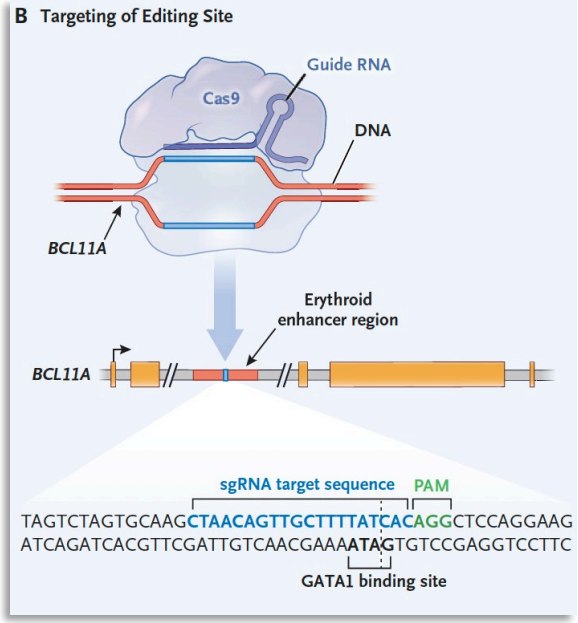
Editas Medicine Granted FDA Regenerative Medicine Advanced Therapy (RMAT) Designation for EDIT-301 for the Treatment of Severe Sickle Cell Disease

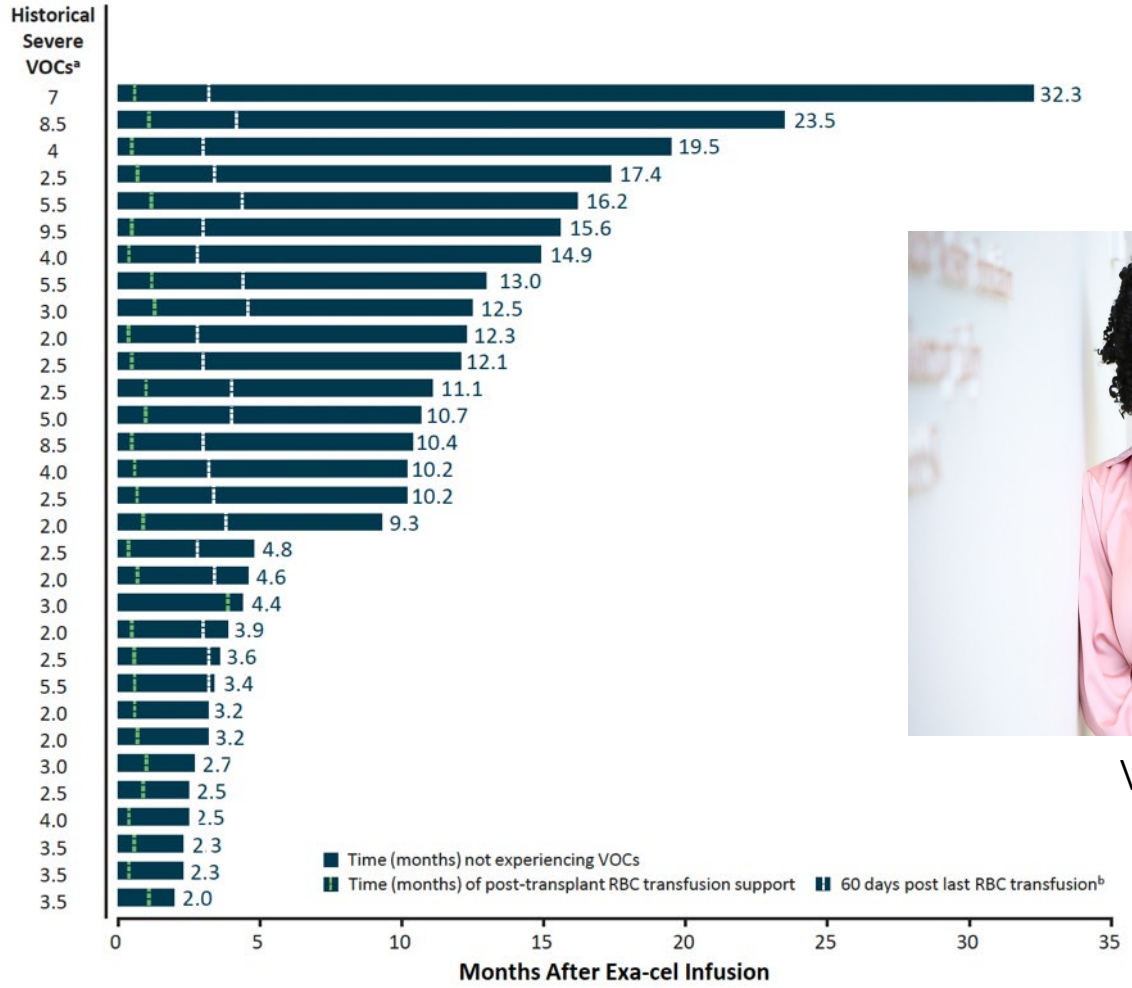
CAMBRIDGE, Mass., Oct. 16, 2023 (GLOBE NEWSWIRE) -- Editas Medicine, Inc. (Nasdaq: EDIT), a clinical-stage genome editing company, today announced that the U.S. Food and Drug Administration (FDA) granted Regenerative Medicine Advanced Therapy (RMAT) designation to EDIT-301, an investigational, gene editing medicine, for the treatment of severe sickle cell disease (SCD).

2022:

CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia

H. Frangoul, D. Altshuler, M.D. Cappellini, Y.-S. Chen, J. Domm, B.K. Eustace, J. Foell, J. de la Fuente, S. Grupp, R. Handgretinger, T.W. Ho, A. Kattamis, A. Kernytsky, J. Lekstrom-Himes, A.M. Li, F. Locatelli, M.Y. Mapara, M. de Montalembert, D. Rondelli, A. Sharma, S. Sheth, S. Soni, M.H. Steinberg, D. Wall, A. Yen, and S. Corbacioglu





Victoria Gray

Franco Locatelli,[1] Haydar Frangoul,[2] Selim Corbacioglu,[3] Josu de la Fuente,[4] Donna Wall,[5] Maria Domenica Cappellini,[6] Mariane de Montalembert,[7] Antonis Kattamis,[8] Stephan Lobitz,[9] Damiano Rondelli,[10] Sujit Sheth,[11] Martin Steinberg,[12] Mark C. Walters,[13] Yael Bobruff,[14] Chris Simard,[14] Yang Song,[14] Lanju Zhang,[14] Anjali Sharma,[15] Suzan Imren,[14] Bill Hobbs,[14] Stephan Grupp[16] on behalf of the CLIMB THAL-111 and CLIMB SCD-121 teams

An Open IND for Point Mutation Repair in HSPCs:
sole all-academic such IND in the entire field of editing

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

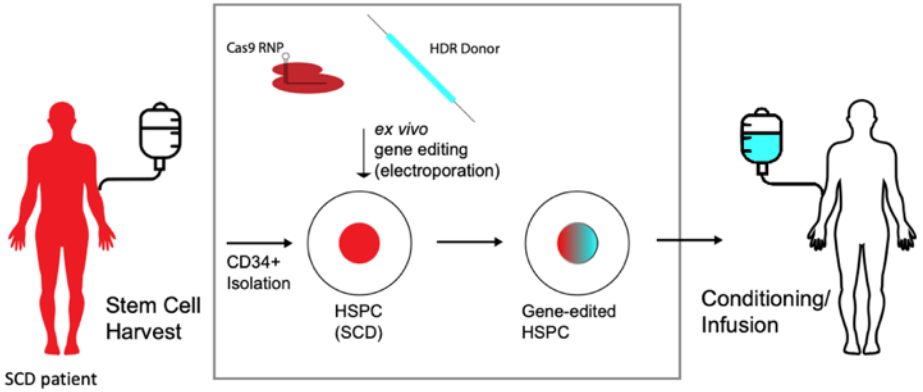
SICKLE CELL DISEASE

Selection-free genome editing of the sickle mutation in human adult hematopoietic stem/progenitor cells

Mark A. DeWitt,[1,2] Wendy Magis,[3] Nicolas L. Bray,[1,2] Tianjiao Wang,[1,2] Jennifer R. Berman,[4] Fabrizia Urbinati,[5] Seok-Jin Heo,[3] Therese Mitros,[2] Denise P. Muñoz,[3] Dario Boffelli,[3] Donald B. Kohn,[5] Mark C. Walters,[3,6] Dana Carroll,[1,7]* David I. K. Martin,[3]* Jacob E. Corn[1,2]*

Dr Mark Walters (UCSF)

Dr Donald Kohn (UCLA)



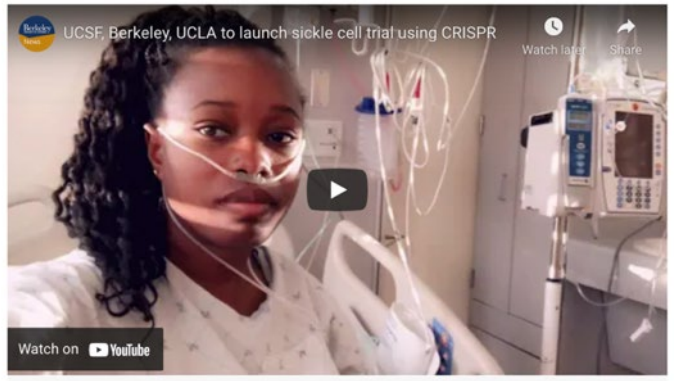
CIRM
CALIFORNIA'S STEM CELL AGENCY

Berkeley News Research People Campus & community

MIND & BODY, RESEARCH

FDA approves first test of CRISPR to correct genetic defect causing sickle cell disease

By Robert Sanders, Media relations | MARCH 30, 2021



2020-2021 Global Survey on Primary Immunodeficiencies

GLOBAL TOTALS

1. Total number of patients being followed	[redacted]
2. Total number of patients identified with a specific PI defect	112,337
3. Total number of patients receiving IgG:	
A) IVIG - Clinic	18,913
B) IVIG - Home	3,344
C) SCIG	13,548
D) Other	256
4. Total number of patients treated by Gene Therapy	248
5. Total number of patients treated with PEG-ADA	126

6. Total number of patients treated by Transplant	6,991
Donor Type:	
A) MRD	1,908
B) MUD	2,012
C) mMUD	462
D) Parental Haplo	1,106
Stem Cell Source:	
A) BM	3,312
B) PBSC	1,334
C) Cord	661
D) Other (please specify)	127

For Tables I - X, please enter the number of patients followed in the box to the right of the specified gene. Available OMIM numbers are provided and linked within each table.

TABLE I. IMMUNODEFICIENCIES AFFECTING CELLULAR AND HUMORAL IMMUNITY

1. ADA (Adenosine deaminase deficiency), AR	OMIM 608958	1.	575	31. LIG4 (DNA ligase IV deficiency), AR	OMIM 601837	31.	60
2. AK2 (AK2 Defect), AR	OMIM 103020	2.	42	32. MALT1 (MALT1 deficiency), AR	OMIM 615468	32.	23
3. B2M (MHC class I deficiency), AR	OMIM 109700	3.	11	33. MAP3K14 (NIK deficiency), AR	OMIM 604655	33.	1
4. BCL10 (BCL10 deficiency), AR	OMIM 616098	4.	4	34. MSN (Moesin deficiency), XL	OMIM 300988	34.	11
5. CARD 11 (CARD11 deficiency), AR LOF	OMIM 615206	5.	31	35. NHEJ1 (Cernunnos/XLF deficiency), AR	OMIM 611290	35.	27
6. CD3D (CD3$_{\delta}$ deficiency), AR	OMIM 186790	6.	54	36. POLD 1 (Polymerase δ deficiency), AR	OMIM 174761	36.	5
7. CD3E (CD3ε deficiency), AR	OMIM 186830	7.	26	37. POLD 2 (Polymerase δ deficiency), AR	OMIM 600815	37.	2
8. CD3G (CD3γ deficiency), AR	OMIM 186740	8.	13	38. PRKDC (DNA PKcs deficiency), AR	OMIM 615966	38.	17
9. CD3Z (CD3ζ deficiency), AR	OMIM 186780	9.	6	39. PTPRC (CD45 Deficiency), AR	OMIM 151460	39.	6
10. CD40 (CD40 deficiency), AR	OMIM 606843	10.	104	40. RAC2 (Activated RAC2 defect), AD GOF	OMIM 602049	40.	13
11. CD40LG (CD40 ligand (CD154) deficiency), XL	OMIM 308230	11.	686	41. RAG1 (RAG deficiency), AR	OMIM 179615	41.	513
12. CD8A (CD8 deficiency), AR	OMIM 186910	12.	18	42. RAG2 (RAG deficiency), AR	OMIM 179616	42.	325
13. CIITA (MHC class II deficiency group A, B, C, D), AR	OMIM 600005	13.	97	43. REL (c-Rel deficiency), AR	OMIM 164910	43.	2
14. CORO1A (Coronin-1A deficiency), AR	OMIM 605000	14.	15	44. RELA (RelA haploinsufficiency), AD	OMIM 618287	44.	7
15. DCLRE1C (Artemis deficiency), AR	OMIM 605988	15.	268	45. RELB (RelB deficiency), AR	OMIM 604758	45.	15
16. DOCK2 (DOCK2 deficiency), AR	OMIM 603122	16.	21	46. RFX5 (MHC class II deficiency group A, B, C, D), AR	OMIM 601863	46.	61
17. DOCK8 (DOCK8 deficiency)), AR	OMIM 243700	17.	509	47. RFXANK (MHC class II deficiency group A, B, C, D), AR	OMIM 603200	47.	156
18. FCHO1 (FCHO1 deficiency), AR	OMIM 613437	18.	10	48. RFXAP (MHC class II deficiency group A, B, C, D), AR	OMIM 601861	48.	16
19. ICOS (ICOS deficiency), AR	OMIM 604558	19.	28	49. RHOH (RHOH deficiency), AR	OMIM 602037	49.	3
20. ICOSLG (ICOSL deficiency), AR	OMIM 605717	20.	3	50. STK4 (MST1 deficiency), AR	OMIM 614868	50.	17
21. IKBKB (IKBKB deficiency), AR	OMIM 615592	21.	32	51. TAP1 (MHC class I deficiency), AR	OMIM 170260	51.	22
22. IKZF1 (IKAROS deficiency), AD DN	OMIM 603023	22.	35	52. TAP2 (MHC class I deficiency), AR	OMIM 170261	52.	6
23. IL21 (IL-21 deficiency), AR	OMIM 615767	23.	2	53. TAPBP (MHC class I deficiency), AR	OMIM 601962	53.	0
24. IL21R (IL-21R deficiency), AR	OMIM 615207	24.	21	54. TFRC (TFRC deficiency), AR	OMIM 616740	54.	15
25. IL2RG ($_{\gamma}$c Deficiency, γc SCID, CD132 deficiency), XL	OMIM 308380	25.	818	55. TNFRSF4 (OX40 deficiency), AR	OMIM 615593	55.	0
26. IL7R (IL7R$_{\alpha}$ deficiency), AR	OMIM 146661	26.	208	56. TRAC (TCR$_{\alpha}$ deficiency), AR	OMIM 615387	56.	9
27. ITK (ITK deficiency), AR	OMIM 186973	27.	34	57. ZAP70 (ZAP-70 combined mutations), AR (LOF/GOF)	OMIM 617006	57.	8
28. JAK3 (JAK3 deficiency), AR	OMIM 600173	28.	250	58. ZAP70 (ZAP-70 deficiency (ZAP70 LOF)), AR	OMIM 269840	58.	103
29. LAT (LAT deficiency), AR	OMIM 602354	29.	1	59. Other Immunodeficiencies Affecting Cellular and Humoral Immunity:		59.	2,160
30. LCK (LCK deficiency), AR	OMIM 615758	30.	3			TOTAL	7,528

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D) Parental Haplo	1,106
Stem Cell Source:	
A) BM	3,312
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C) Cord	661
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505 different inborn errors of immunity

>112,000 patients

ZERO gene editing trials for them

ONE approved gene therapy product

JEM Journal of Experimental Medicine

BRIEF DEFINITIVE REPORT

Inherited SLP76 deficiency in humans causes severe combined immunodeficiency, neutrophil and platelet defects

Atar Lev[1,2], Yu Nee Lee[1], Guangping Sun[3], Enas Hallumi[4], Amos J. Simon[1,5], Keren S. Zrihen[1], Shiran Levy[1], Tal Beit Halevi[1], Maria Papazian[1], Neta Shwartz[1], Ido Somekh[6], Sarina Levy-Mendelovich[7], Baruch Wolach[8], Ronit Gavrieli[8], Helly Vernitsky[5], Ortal Barel[9,12], Elisheva Javasky[9,12], Tali Stauber[1], Chi A. Ma[3], Yuan Zhang[3,10], Ninette Amariglio[2,11], Gideon Rechavi[12,13], Ayal Hendel[2], Deborah Yablonski[4], Joshua D. Milner[3,10]*, and Raz Somech[1,13]*

[1]Pediatric Department A and Immunology Service, Jeffrey Modell Foundation Center, Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Tel Hashomer, Israel; [2]The Mina and Everard Goodman Faculty of Life Sciences, Advanced Materials and Nanotechnology Institute, Bar-Ilan University, Ramat Gan, Israel; [3]Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD; [4]Department of Immunology, Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel; [5]Division of Haematology and Bone Marrow Transplantation, Sheba Medical Center, Tel Hashomer, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [6]Department of Pediatric Hematology Oncology, Schneider Children's Medical Center of Israel, Petah Tikva, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [7]The Israeli National Hemophilia Center and Thrombosis Unit, The Amalia Biron Research Institute of Thrombosis and Hemostasis, Sheba Medical Center, Tel Hashomer, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; [8]Department of Pediatrics and Laboratory for Leukocyte Function, Meir Medical Center, Kfar Saba, Israel; [9]The Genomic Unit, Sheba Cancer Research Center, Sheba Medical Center, Tel Hashomer, Israel; [10]Department of Pediatrics, Columbia University Irving Medical Center, New York, NY; [11]Cancer Research Center, Sheba Medical Center, Tel Hashomer, Ramat Gan, Israel; [12]Cancer Research Center, Wohl Institute for Translational Medicine, Sheba Medical Center, Tel Hashomer, Israel; [13]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

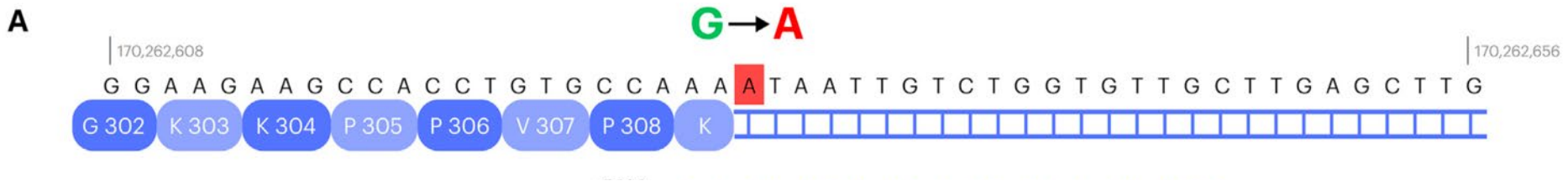
"[Patient] presented at the age of 2 mo with recurrent skin abscesses and skin rash.

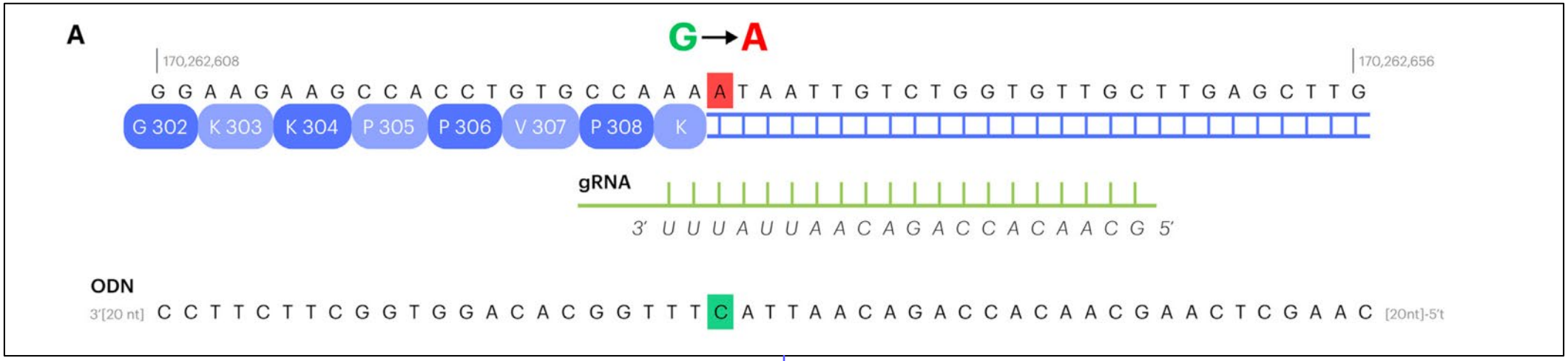
The patient died of transplant-related complications [at 10 months of age]."

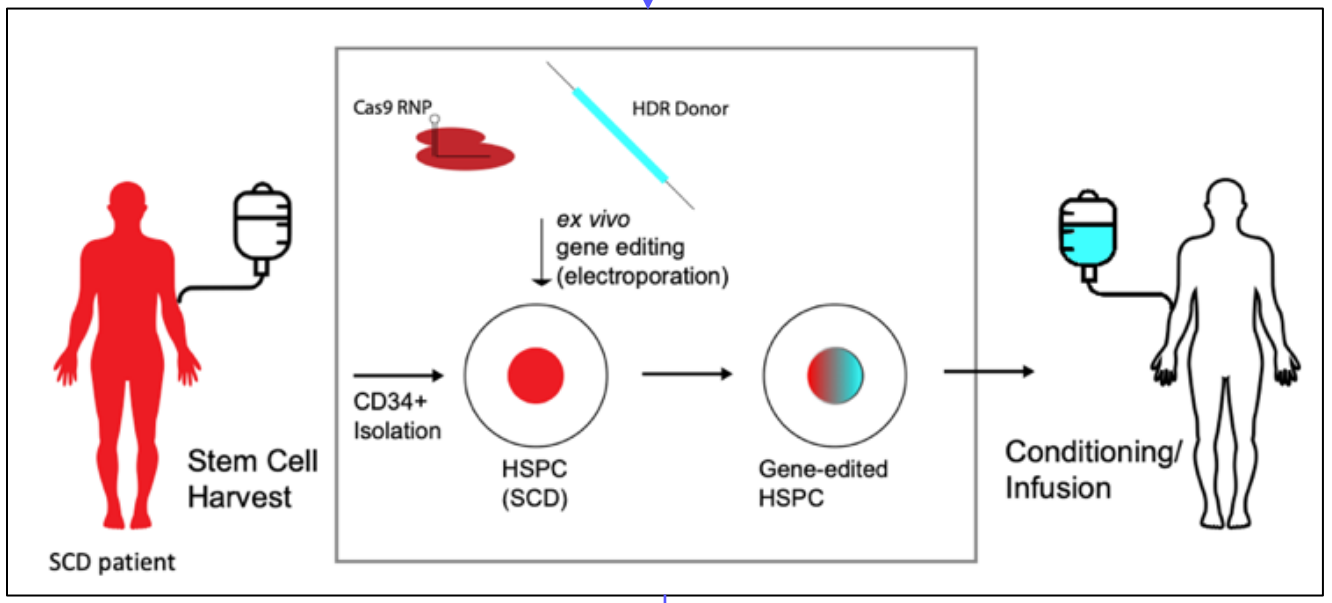
What killed this child?

a novel mutation in the *SLP76* gene

The mutation that killed this child was actionably editable





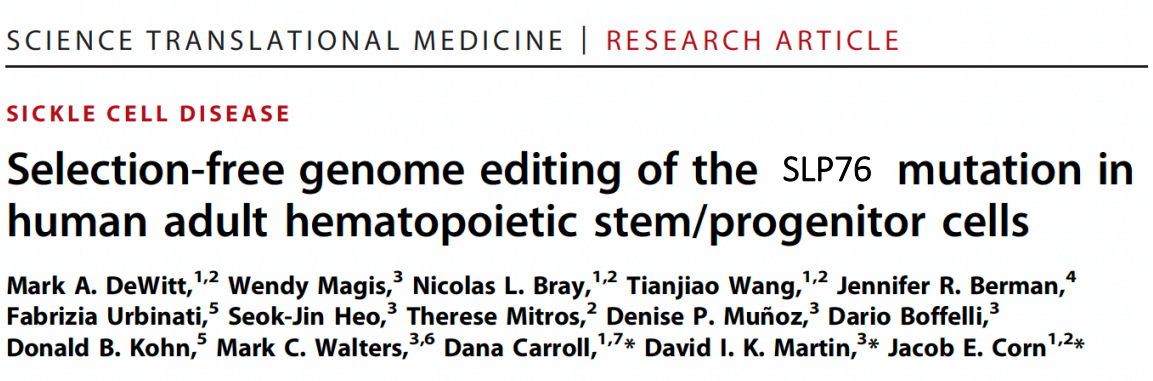


TWO MONTHS from mutation to clinical lead ready to go

ONE MONTH to make+release cell product

3 months to clinical outcome

If you change something – eg the gRNA and the ssODN – it's a new product, so back to square 1



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

SICKLE CELL DISEASE

Selection-free genome editing of the SLP76 mutation in human adult hematopoietic stem/progenitor cells

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Patient → Cause → Effector → Efficacy → Safety → CMC → Regulatory → Trial

~ 4 years, $7m (academic pricing)

~ 4 years, $7m (academic pricing)

Gap #1:

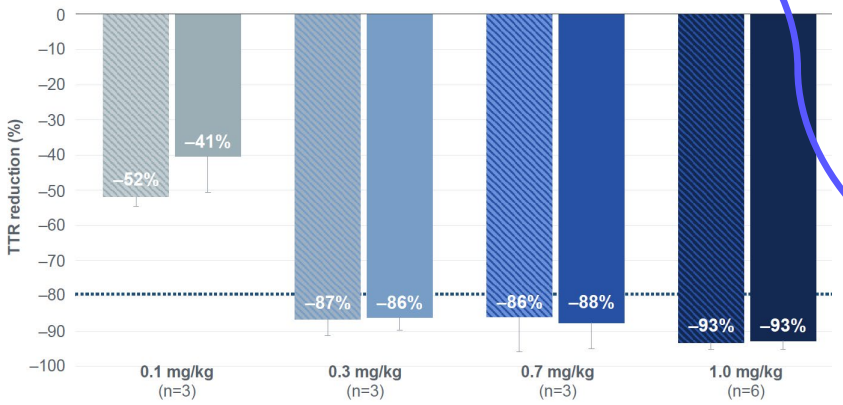
Rapid progress in genome-editing two blood diseases (SCD+TDT) has, at present, no path to affecting 112,000 patients with editable blood disease

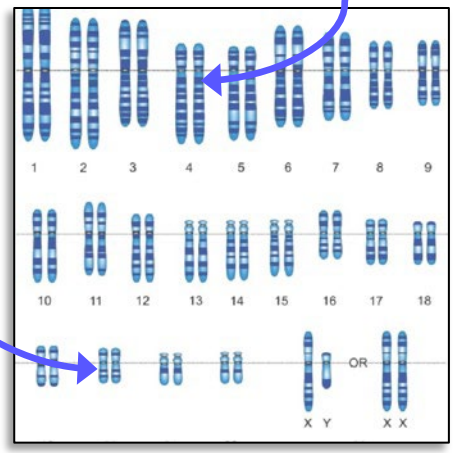
2022: Intellia Therapeutics reducing the “CRISPR is a therapeutic platform” vision to clinical practice

CRISPR-Cas9 can be programmed to cut a specific sequence of DNA in patients with entirely different diseases by changing the guide RNA

Disease 1: TTR Amyloidosis

Gene: ATTR on chr 20a

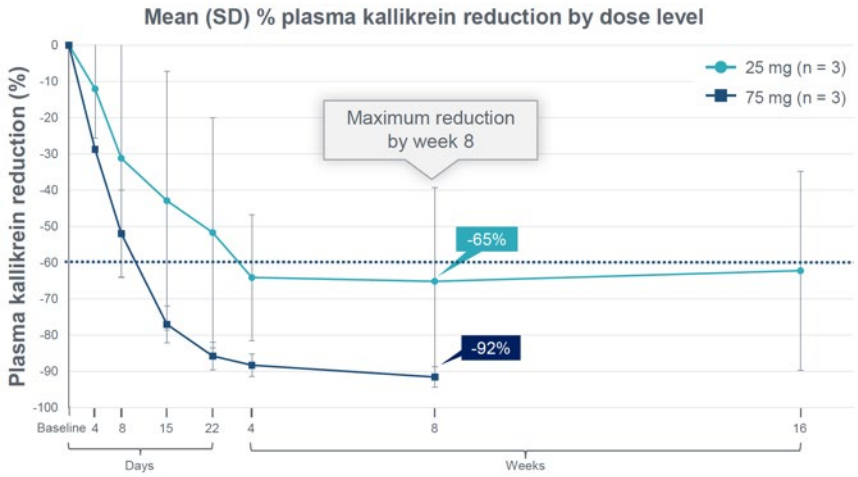




93% target gene knockout in patient liver

Disease 2: Hereditary Angioedema

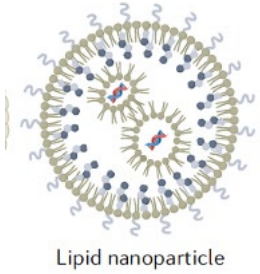
Gene: KLKB1 on chr 4



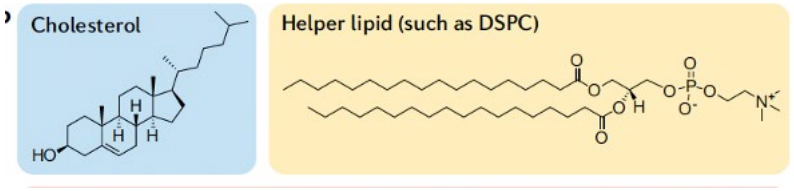
92% target gene knockdown in patient liver

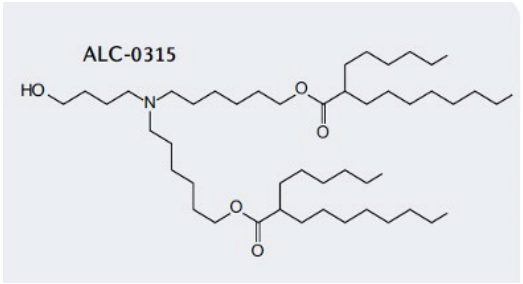
In vivo mRNA delivery via LNP technology has been scaled to the entirety of the Earth's population

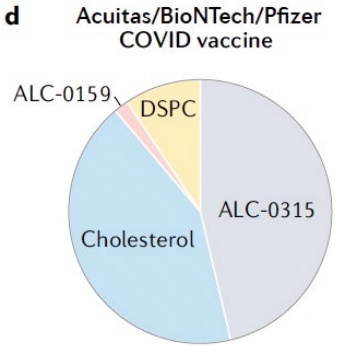
Paunovska *NatRevGenet* 2022

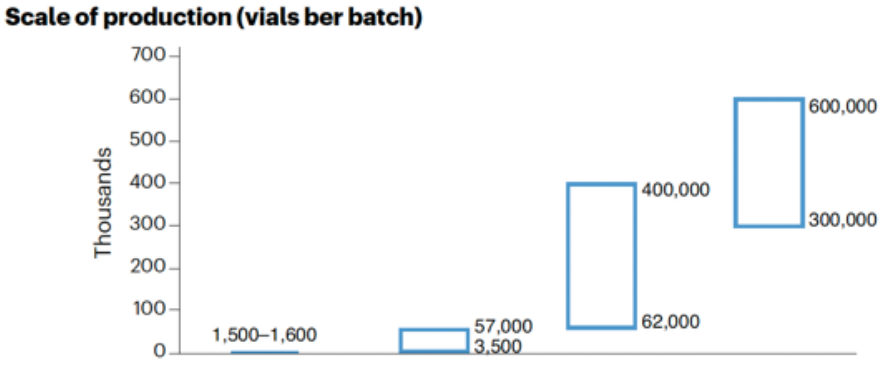


Lipid nanoparticle









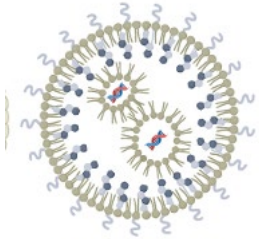
Process step	Phase 1	Phase 3/pivotal	Initial launch	2021 scale-up
Plasmid	PCR	PCR	Plasmid DNA	Plasmid DNA
mRNA DS	1 g	1–5 g	10 g	250 g–1 kg
DP (volume)			125 L	1,600 L

Fig. 2 | COVID-19 vaccine production scale. The scale of plasmid, mRNA drug substance (DS) and drug product (DP) production increased up to 1,000-fold.

Pfizer CMC:

A kilogram of GMP mRNA

3,000,000,000 doses of LNP-mRNA



Lipid nanoparticle

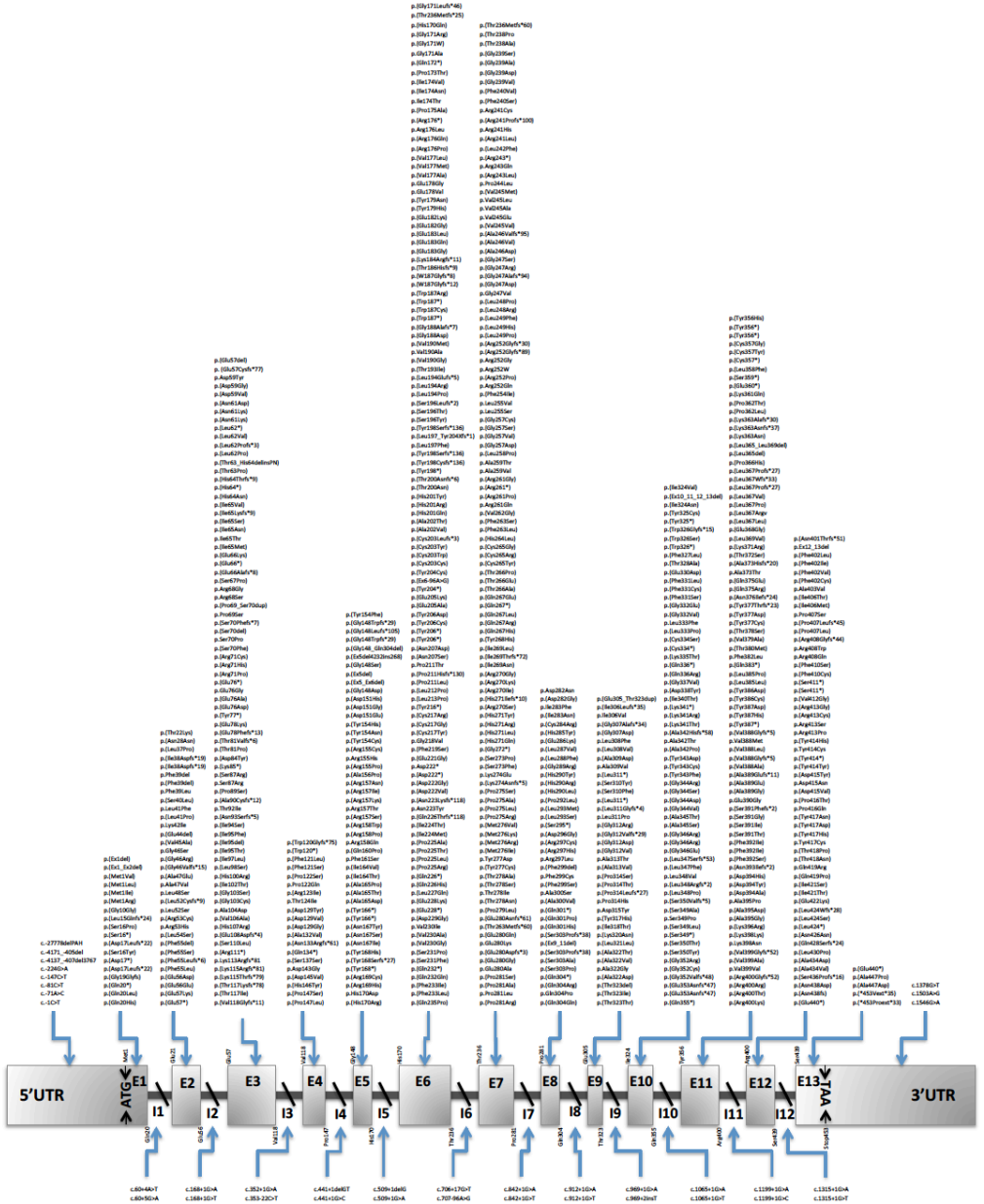
Phenylketonuria:

1 in 15,000 live births in the US

Over 90% of the newborns could be CRISPR-gene-edited to health in their first year of life using EXISTING technologies.

No clinical trials for editing in PKU …

… to say nothing about the 2,500 newborns in US per year with IEMs.

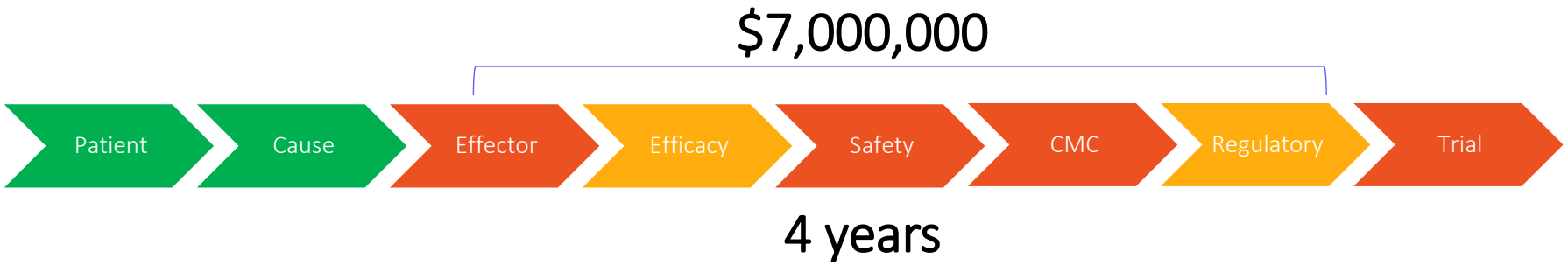


http://www.biopku.org/home/docs/variants_all.pdf
https://depts.washington.edu/pku/about/diet.html

Gap #2:

Rapid progress in genome-editing the liver for two diseases (ATTR and HAE) has, at present, no path to affecting >2,500 US newborns per year with inborn errors of metabolism

The current nonclinical pharmtox, CMC, and regulatory framework need an upgrade to align with the clinically established platform nature of CRISPR-Cas genome editing AND the unmet medical need in “rare” diseases.


$7,000,000
Patient
Cause
Effector
Efficacy
Safety
CMC
Regulatory
Trial
4 years


Patient
Cause
Effector
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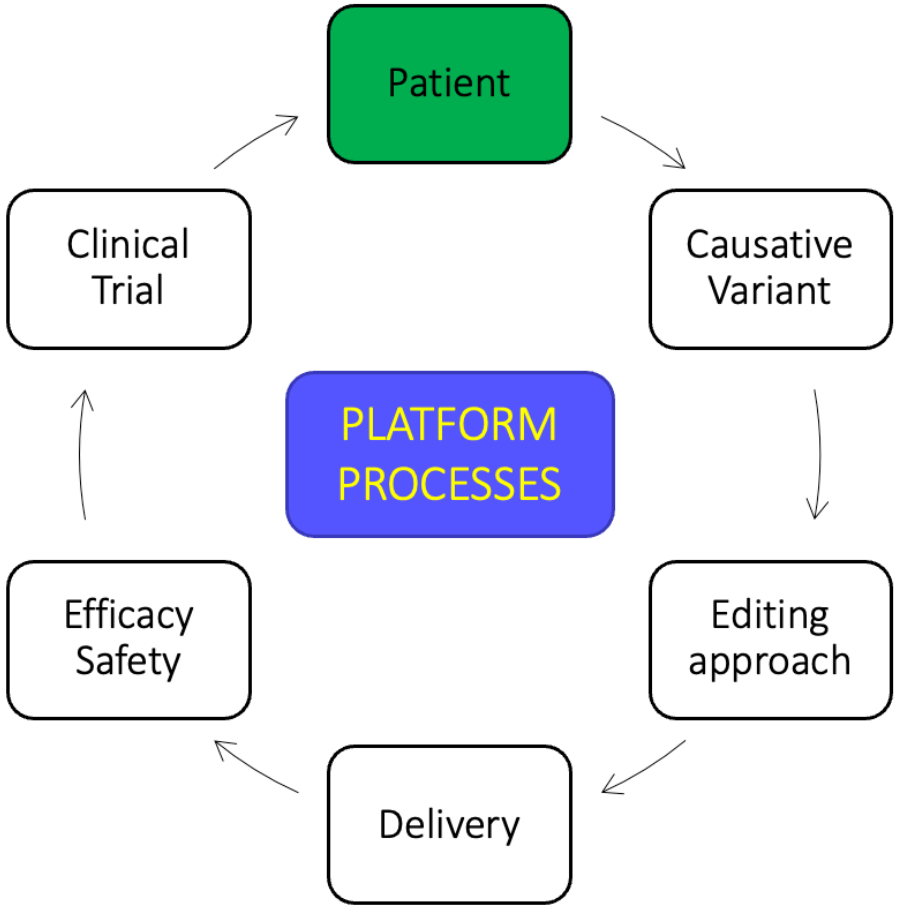
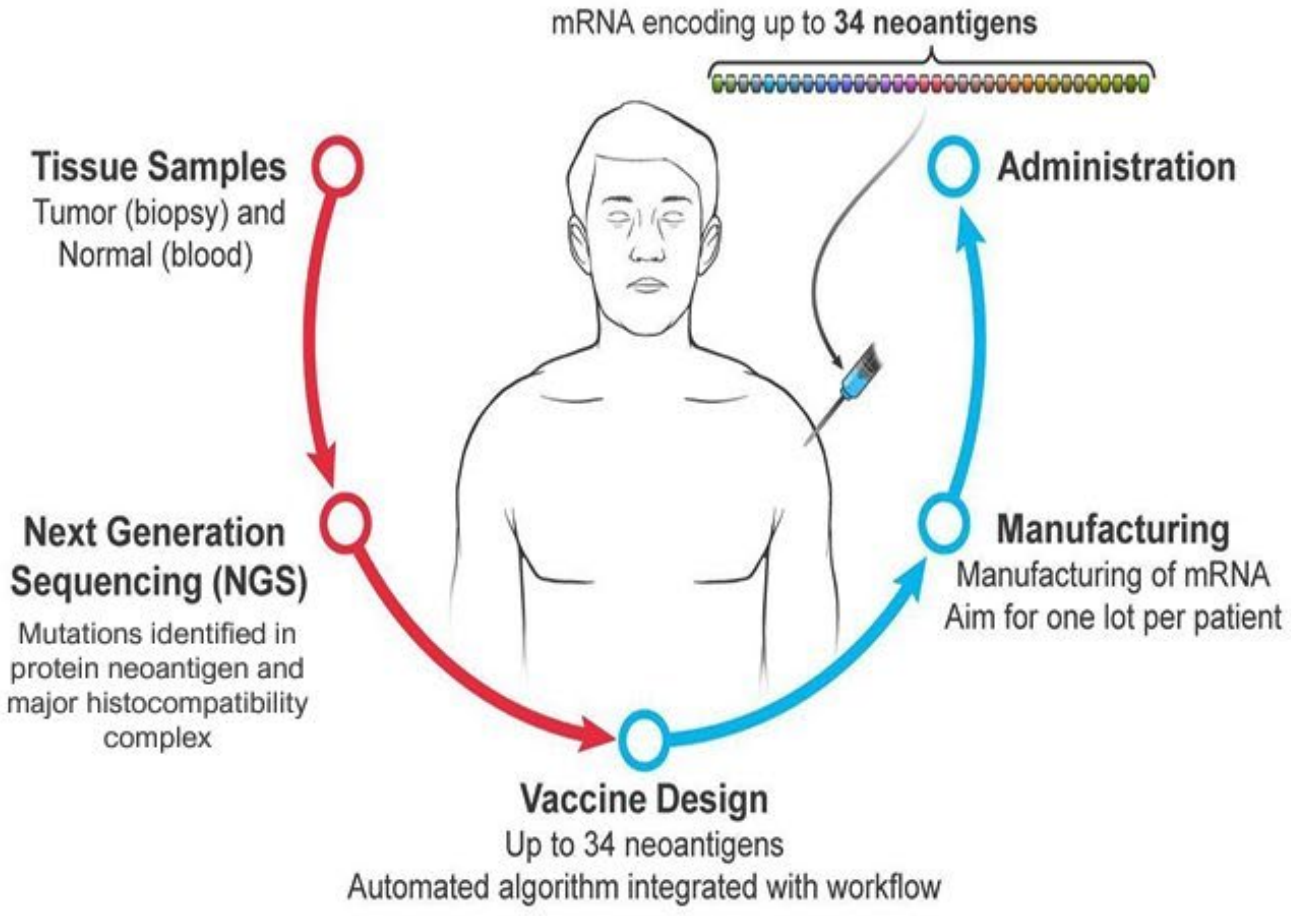
Regulatory
Trial


Patient
Causative Variant
Editing approach
Delivery
Efficacy Safety
Clinical Trial
PLATFORM PROCESSES

MERCK

Personalized cancer vaccine (mRNA-4157)

Designed to target an individual patient's unique tumor mutations



Personalized drug design

Rapid turnaround times

Needle-to-needle in just **weeks**

moderna

CRISPR Catch-2023:

The only way to find out how to safely and efficiently genome-edit people is

to edit more people.

This requires new nonclinical frameworks to take editing to clinic.

This, in turn, requires more clinical data on what matters and what does not

at the nonclinical stage.

Not enough clinical data because current path to IND is long and expensive. If there were more clinical data we'd improve it.
But we cannot improve it because that current path is, itself, an obstacle to improving it.

CRISPR Cures 2033?

2020-2021 Global Survey on Primary Immunodeficiencies

GLOBAL TOTALS

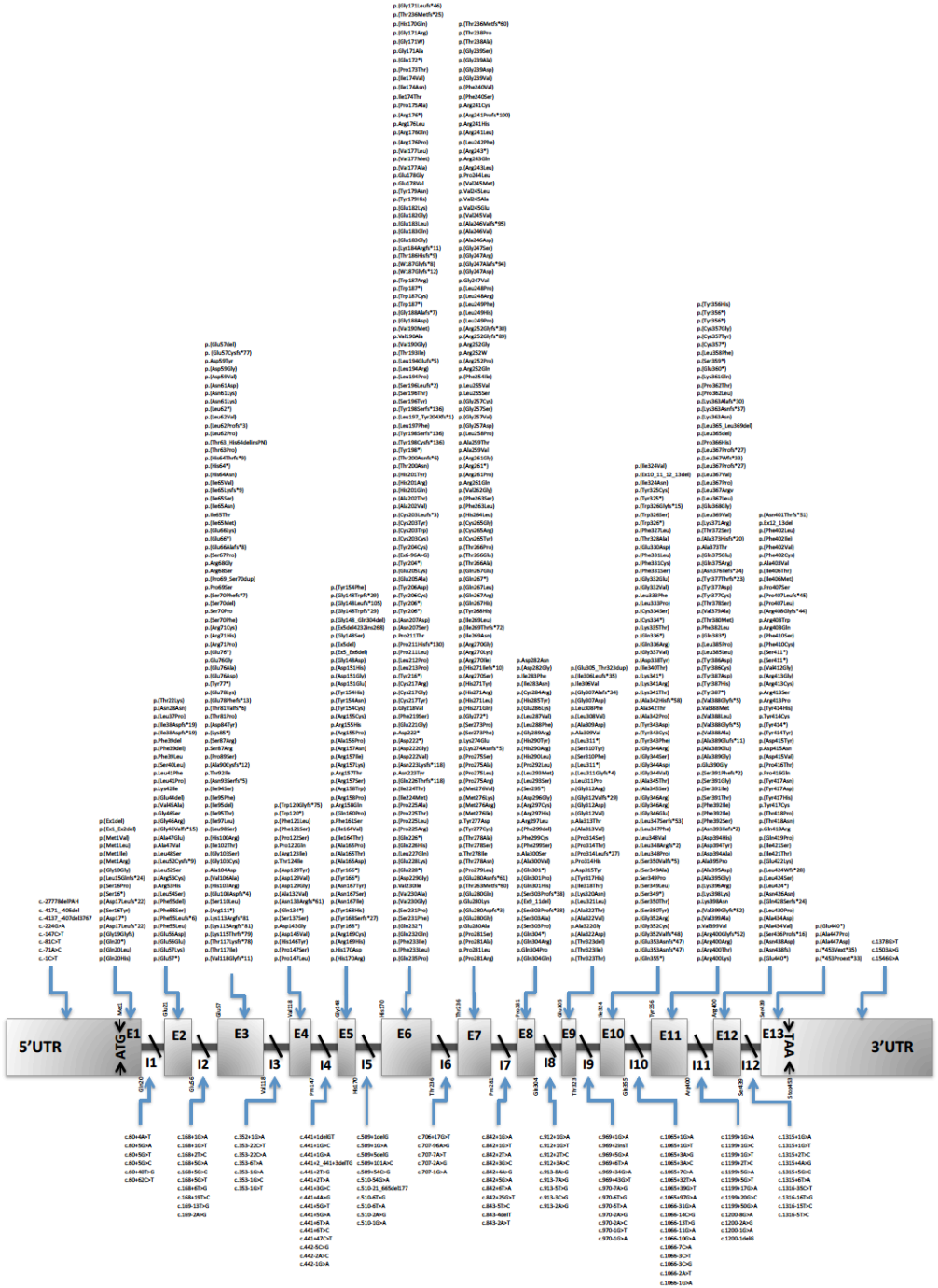
Jeffrey Modell Centers Network

1. Total number of patients being followed	256,153	6. Total number of patients treated by Transplant	6,991
2. Total number of patients identified with a specific PI defect	112,337	Donor Type:	
3. Total number of patients receiving IgG:		A) MRD	1,908
A) IVIG - Clinic	18,913	B) MUD	2,012
B) IVIG - Home	3,344	C) mMUD	462
C) SCIG	13,548	D) Parental Haplo	1,106
D) Other	256	Stem Cell Source:	
4. Total number of patients treated by Gene Therapy	248	A) BM	3,312
5. Total number of patients treated with PEG-ADA	126	B) PBSC	1,334
		C) Cord	661
		D) Other (please specify)	127

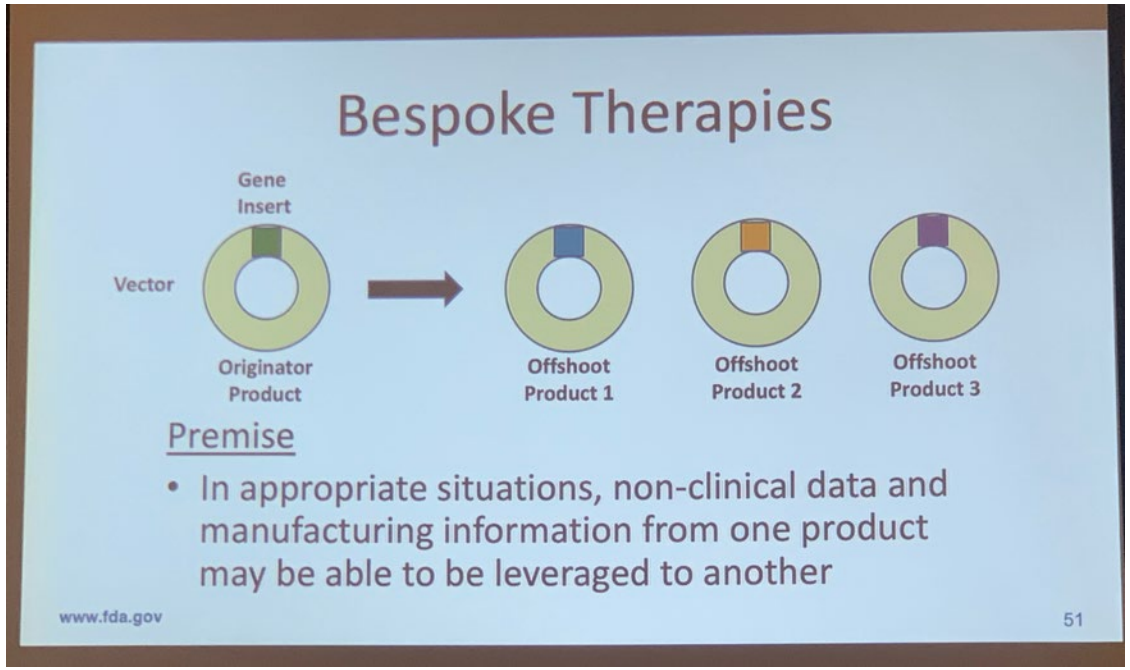
For Tables I - X, please enter the number of patients followed in the box to the right of the specified gene. Available OMIM numbers are provided and linked within each table.

TABLE I. IMMUNODEFICIENCIES AFFECTING CELLULAR AND HUMORAL IMMUNITY

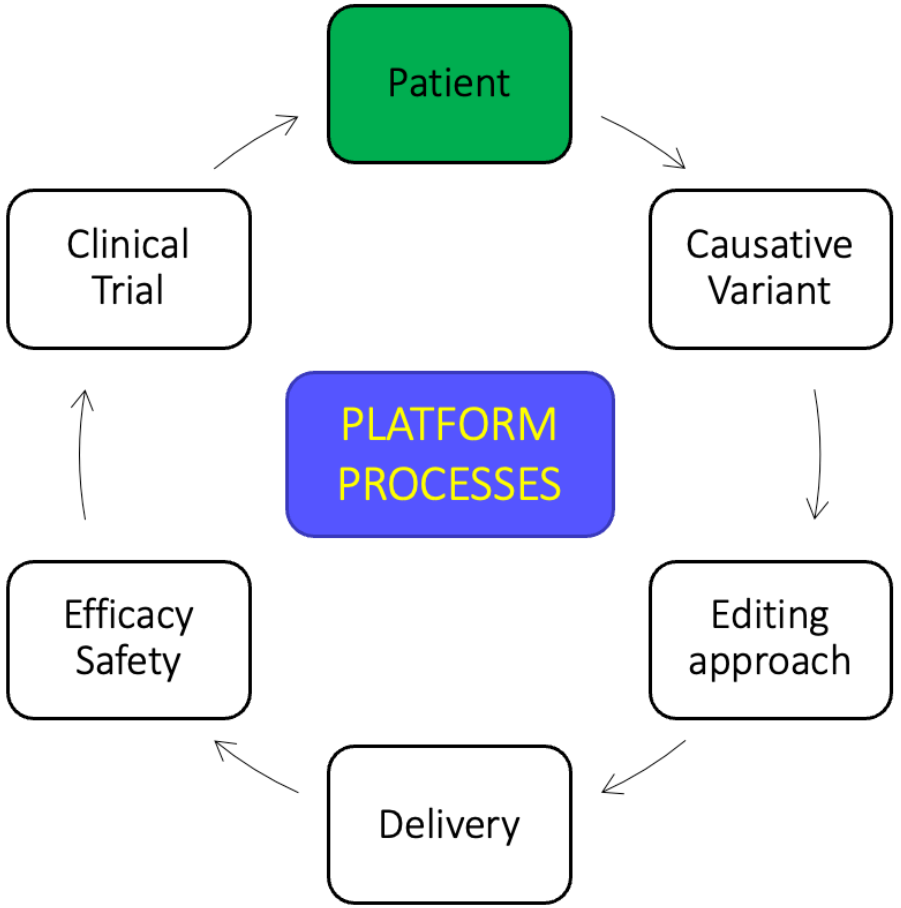
1. ADA (Adenosine deaminase deficiency), AR	OMIM 608958	1.	575	31. LIG4 (DNA ligase IV deficiency), AR	OMIM 601837	31.	60
2. AK2 (AK2 Defect), AR	OMIM 103020	2.	42	32. MALT1 (MALT1 deficiency), AR	OMIM 615468	32.	23
3. B2M (MHC class I deficiency), AR	OMIM 109700	3.	11	33. MAP3K14 (NIK deficiency), AR	OMIM 604655	33.	1
4. BCL10 (BCL10 deficiency), AR	OMIM 616098	4.	4	34. MSN (Moesin deficiency), XL	OMIM 300988	34.	11
5. CARD 11 (CARD11 deficiency), AR LOF	OMIM 615206	5.	31	35. NHEJ1 (Cernunnos/XLF deficiency), AR	OMIM 611290	35.	27
6. CD3D (CD3$_\delta$ deficiency), AR	OMIM 186790	6.	54	36. POLD 1 (Polymerase δ deficiency), AR	OMIM 174761	36.	5
7. CD3E (CD3$_\varepsilon$ deficiency), AR	OMIM 186830	7.	26	37. POLD 2 (Polymerase δ deficiency), AR	OMIM 600815	37.	2
8. CD3G (CD3$_\gamma$ deficiency), AR	OMIM 186740	8.	13	38. PRKDC (DNA PKcs deficiency), AR	OMIM 615966	38.	17
9. CD3Z (CD3$_\zeta$ deficiency), AR	OMIM 186780	9.	6	39. PTPRC (CD45 Deficiency), AR	OMIM 151460	39.	6
10. CD40 (CD40 deficiency), AR	OMIM 606843	10.	104	40. RAC2 (Activated RAC2 defect), AD GOF	OMIM 602049	40.	13
11. CD40LG (CD40 ligand (CD154) deficiency), XL	OMIM 308230	11.	686	41. RAG1 (RAG deficiency), AR	OMIM 179615	41.	513
12. CD8A (CD8 deficiency), AR	OMIM 186910	12.	18	42. RAG2 (RAG deficiency), AR	OMIM 179616	42.	325
13. CIITA (MHC class II deficiency group A, B, C, D), AR	OMIM 600005	13.	97	43. REL (c-Rel deficiency), AR	OMIM 164910	43.	2
14. CORO1A (Coronin-1A deficiency), AR	OMIM 605000	14.	15	44. RELA (RelA haploinsufficiency), AD	OMIM 618287	44.	7
15. DCLRE1C (Artemis deficiency), AR	OMIM 605988	15.	268	45. RELB (RelB deficiency), AR	OMIM 604758	45.	15
16. DOCK2 (DOCK2 deficiency), AR	OMIM 603122	16.	21	46. RFX5 (MHC class II deficiency group A, B, C, D), AR	OMIM 601863	46.	61
17. DOCK8 (DOCK8 deficiency), AR	OMIM 243700	17.	509	47. RFXANK (MHC class II deficiency group A, B, C, D), AR	OMIM 603200	47.	156
18. FCHO1 (FCHO1 deficiency), AR	OMIM 613437	18.	10	48. RFXAP (MHC class II deficiency group A, B, C, D), AR	OMIM 601861	48.	16
19. ICOS (ICOS deficiency), AR	OMIM 604558	19.	28	49. RHOH (RHOH deficiency), AR	OMIM 602037	49.	3
20. ICOSLG (ICOSL deficiency), AR	OMIM 605717	20.	3	50. STK4 (MST1 deficiency), AR	OMIM 614868	50.	17
21. IKBKB (IKBKB deficiency), AR	OMIM 615592	21.	32	51. TAP1 (MHC class I deficiency), AR	OMIM 170260	51.	22
22. IKZF1 (IKAROS deficiency), AD DN	OMIM 603023	22.	35	52. TAP2 (MHC class I deficiency), AR	OMIM 170261	52.	6
23. IL21 (IL-21 deficiency), AR	OMIM 615767	23.	2	53. TAPBP (MHC class I deficiency), AR	OMIM 601962	53.	0
24. IL21R (IL-21R deficiency), AR	OMIM 615207	24.	21	54. TFRC (TFRC deficiency), AR	OMIM 616740	54.	15
25. IL2RG ($_{\gamma c}$ Deficiency, γc SCID, CD132 deficiency), XL	OMIM 308380	25.	818	55. TNFRSF4 (OX40 deficiency), AR	OMIM 615593	55.	0
26. IL7R (IL7R$_\alpha$ deficiency), AR	OMIM 146661	26.	208	56. TRAC (TCR$_\alpha$ deficiency), AR	OMIM 615387	56.	9
27. ITK (ITK deficiency), AR	OMIM 186973	27.	34	57. ZAP70 (ZAP-70 combined mutations), AR (LOF/GOF)	OMIM 617006	57.	8
28. JAK3 (JAK3 deficiency), AR	OMIM 600173	28.	250	58. ZAP70 (ZAP-70 deficiency (ZAP70 LOF)), AR	OMIM 269840	58.	103
29. LAT (LAT deficiency), AR	OMIM 602354	29.	1	59. Other Immunodeficiencies Affecting Cellular and Humoral Immunity:		59.	2,160
30. LCK (LCK deficiency), AR	OMIM 615758	30.	3			TOTAL	7,528



CBER leadership lays out a vision for bespoke therapy acceleration



The IGI is advancing specific instantiations of this to IND



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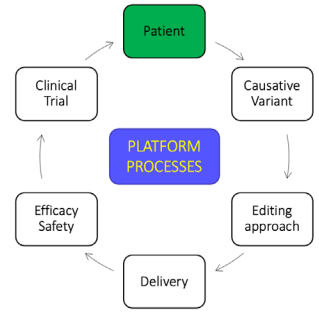
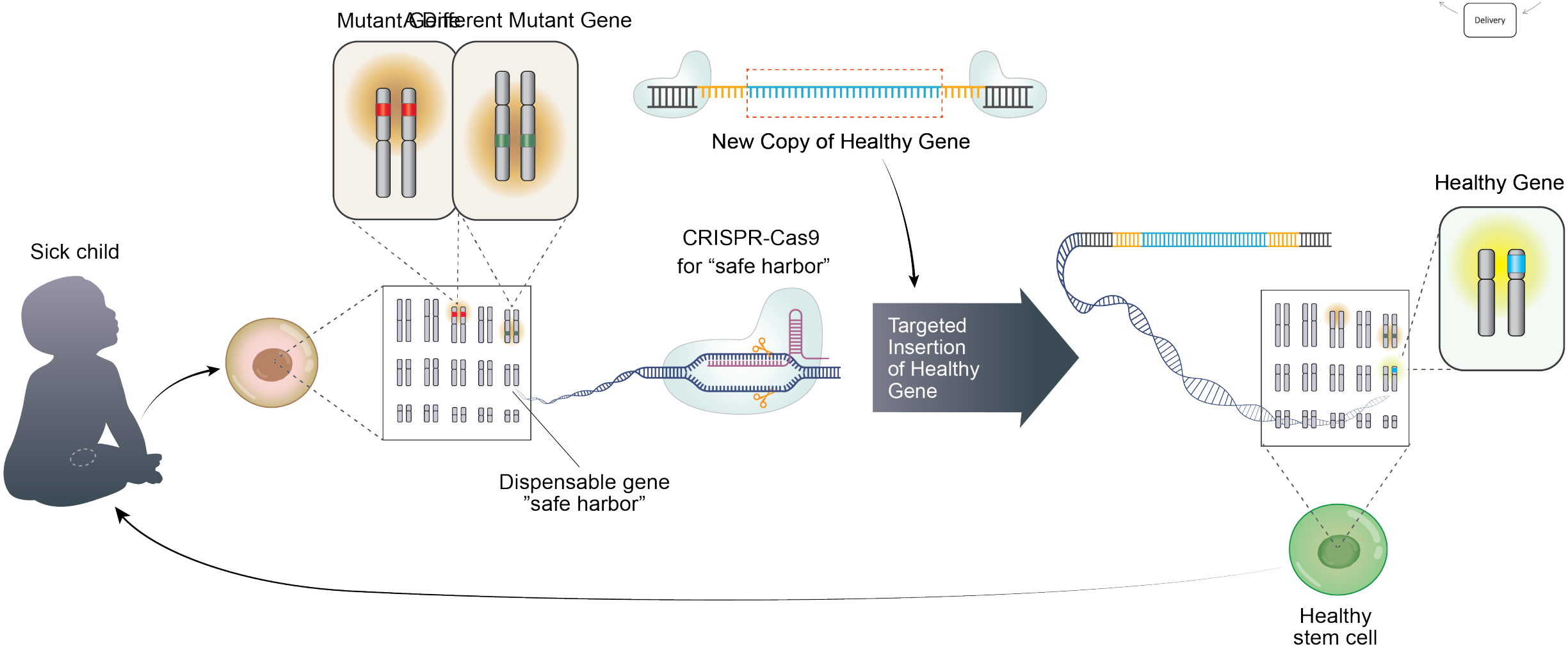
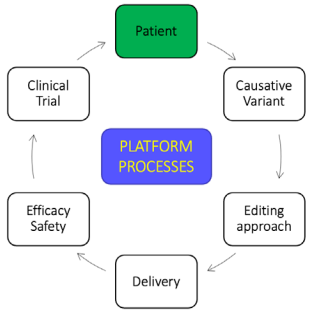




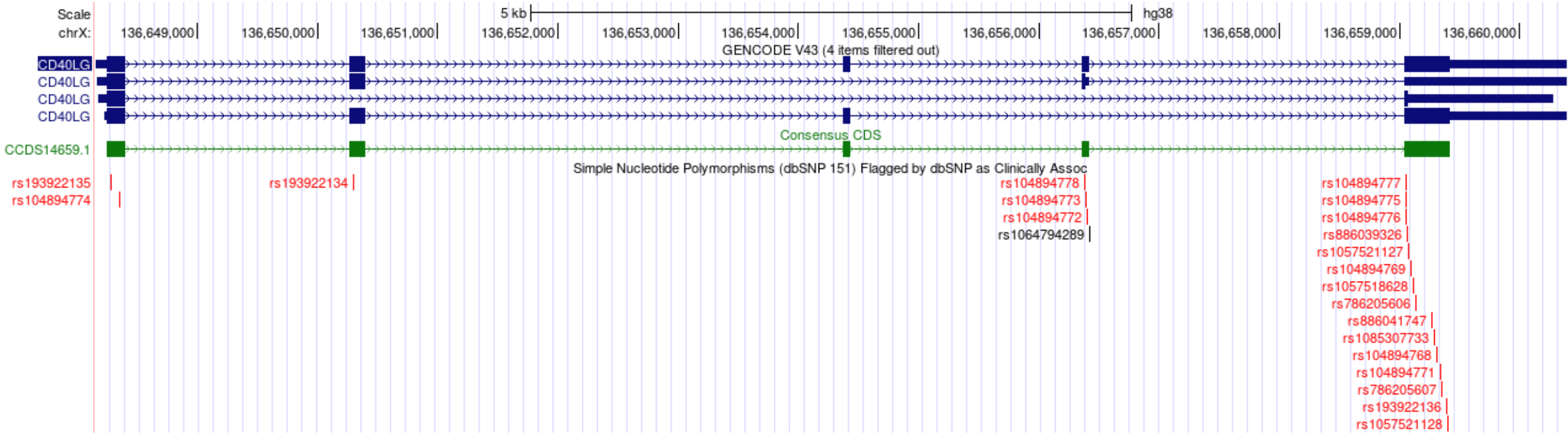
Disease 1 to disease 2: the only component that changes is the single-stranded DNA segment encoding the transgene.

Disease 1 (CIRM support): ARTEMIS-SCID (with Jennifer Puck and Mort Cowan (UCSF) and Donald Kohn (UCLA)

The IGI is advancing specific instantiations of this to IND



CD40 ligand (CD40L) deficiency or X-linked Hyper-IgM syndrome is a severe primary immunodeficiency caused by mutations in the CD40L gene. Despite currently available treatments, CD40L-deficient patients remain susceptible to life-threatening infections and have poor long term survival.

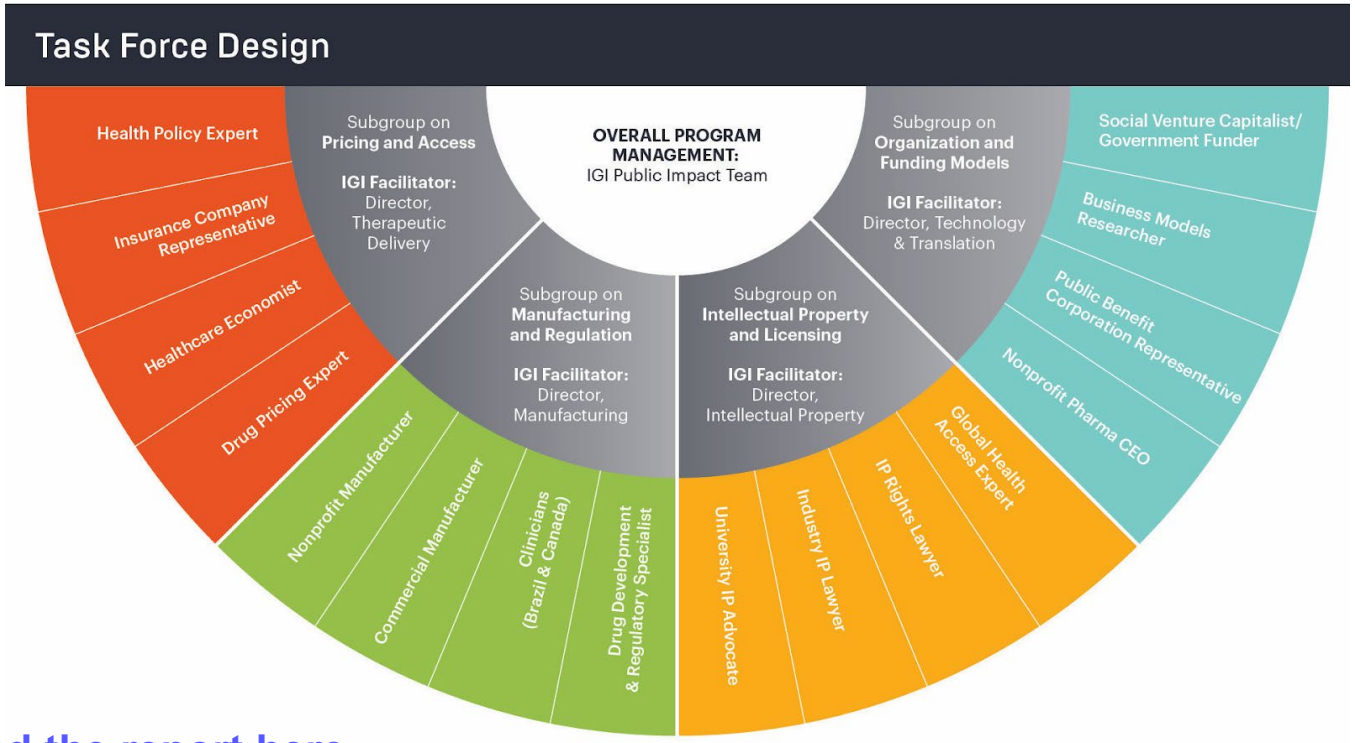


For same disease: different patients, different mutations. The only thing that changes is the gRNA

Diseases 1 and 2: HLH (with Michelle Hermiston, UCSF) and ALSP (with Jeffrey Goldberg and Carlo Condello, UCSF)

An IGI Task Force explored solutions to affordability and access challenges for genomic medicines

innovativegenomics.org/atf-report/



Dynamic cost-plus approach
anchoring price to COGS can drop prices by 10X

Manufacturing Innovation
Point-of-care manufacturing, automation, and platformization

Global access provisions
Empower TTOs to negotiate access into licensing agreements

A tripartite business model
Academic-Nonprofit-Public Benefit Corporation

Find the report here

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