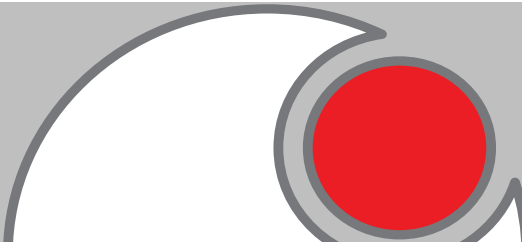


iTOP: CRISPR delivery with a pinch of salt

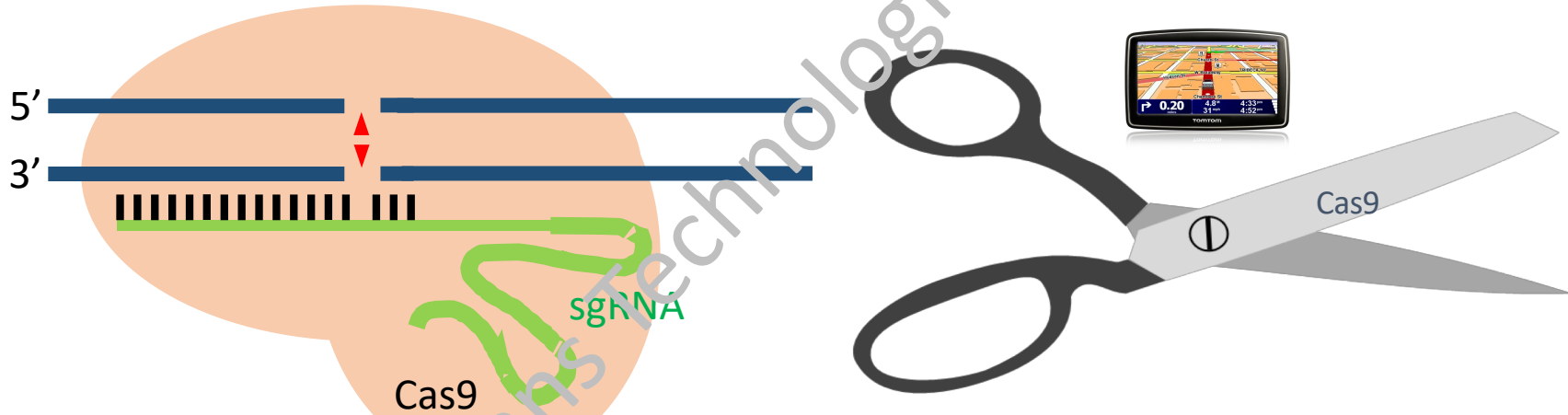
taking gene-editing to the clinic

Dr. Marco de Boer MBA
CEO



Dutch Life Sciences

CRISPR/Cas9, molecular scissors

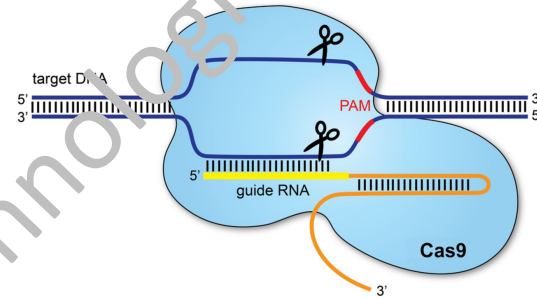


Concept of Gene Editing

CRISPR proteins

GuideRNA

Delivery



The Challenge

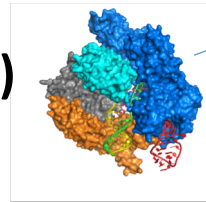
DNA



mRNA



RNP (Ribonucleoproteins)



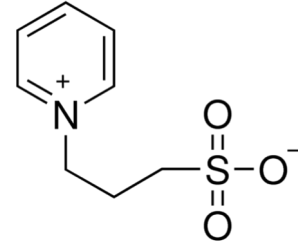
iTOP

Fast in, Fast out !

Viral free delivery of CRISPR-Cas9 *in vitro* and in tissue

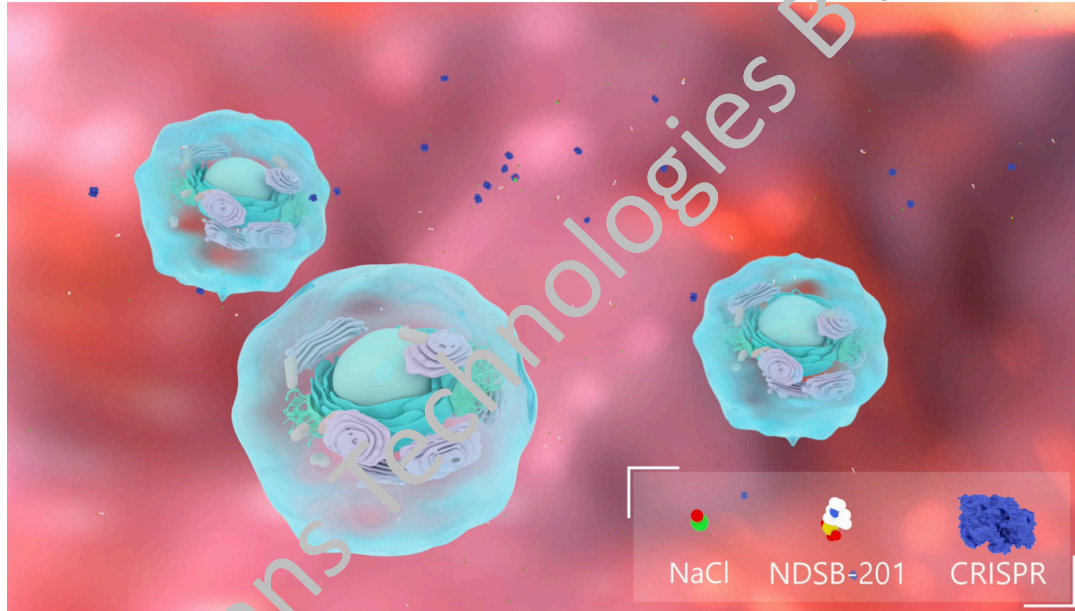
iTGP

Two essential buffer components



NDSB201

How does iTOP work?

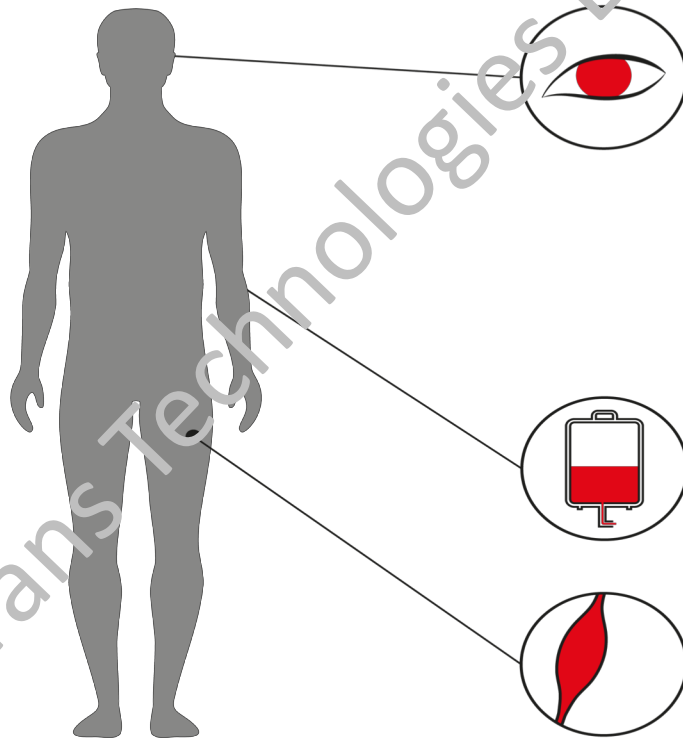


<https://www.ntranstechnologies.com/technology/>

Cell 2015, 161: 674-690

Induced Transduction by Osmocytosis and Propenebetaine

iTOP applications



Challenges of Clinical CRISPR applications

- Off target effects

LETTER

<https://doi.org/10.1038/s41586-018-0500-9>

In vivo CRISPR editing with no detectable genome-wide off-target mutations

Pinar Akcakaya^{1,13}, Maggie L. Bobbin^{2,3,4,13}, Jimmy Guo^{2,3}, Jose Malagon-Lopez^{2,3,4}, Kendell Clement^{2,3,4}, Sara P. Garcia², Mick D. Fellows³, Michelle J. Porritt¹, Mike J. Firsiroti⁶, Alba Carreras^{1,9}, Tania Baccega^{1,10}, Frank Seeliger⁷, Mikael Bjursell¹, Shengdar Q. Tsai^{2,3,4,11}, Nhu T. Nguyen^{2,3}, Roberto Jitsch⁸, Lorenz M. Mayr^{1,12}, Luca Pinello^{2,4}, Mohammad Bohlooly-Y¹, Martin J. Aryee^{2,4}, Marcello Maresca¹⁴, Ken Young^{2,3,4*}

- Immune response

Mol Ther Methods Clin Dev. 2018 Sep 21; 10: 105–112.

Published online 21 Jun 15. doi: [10.1016/j.omtm.2018.06.006](https://doi.org/10.1016/j.omtm.2018.06.006)

PMCID: PMC6070699

PMID: [30073181](https://pubmed.ncbi.nlm.nih.gov/30073181/)

Prevalence of Pre-existing Antibodies to CRISPR-Associated Nuclease Cas9 in the USA Population

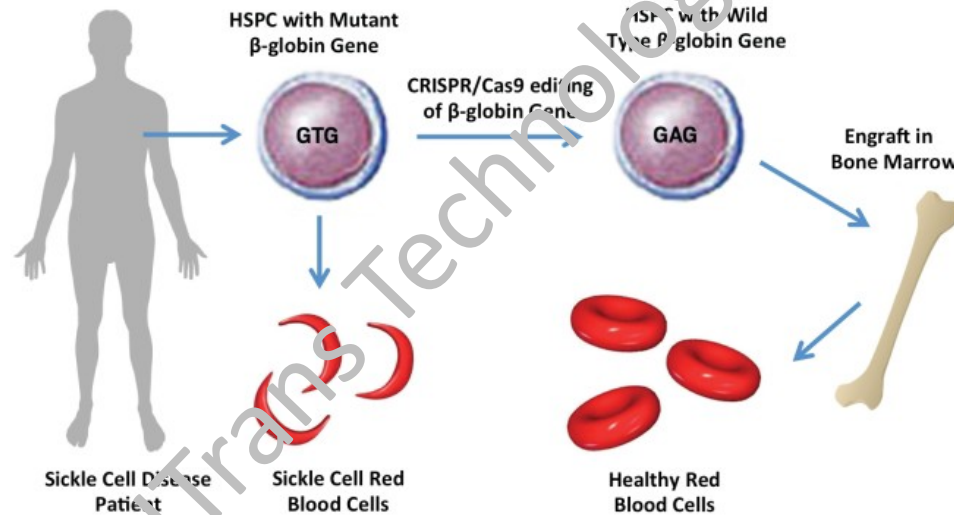
Jiayao L. Simhadri,¹ Joseph McGill,¹ Shane McMahon,¹ Junxia Wang,² Haiyan Jiang,² and Zuben E. Sauna^{1,*}

Staphylococcus aureus (SaCas9) and *Streptococcus pyogenes* (SpCas9): prevalence of antibodies to be **10%** and **2.5%**

First CRISPR Clinical Trial Begins in Europe

Gene-editing technology is revolutionary, but safety and ethical concerns remain

MARCUS BANKS • NOVEMBER 12, 2018



de Volkskrant

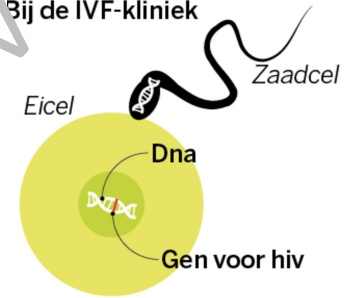
NIEUWS GENTECH

Claim Chinese hoogleraar: eerste genetisch gemanipuleerde baby's ter wereld

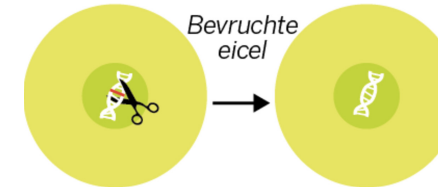


GENETISCH GEMANIPULEERDE BABY

Bij de IVF-kliniek



Met CRISPR-Casetechniek
wordt hiv gen verwijderd



'Gerepareerde'
foetus wordt
geïmplaneerd

Foetus
resistent
tegen hiv

With special thanks to.....

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CRISPR applications

