Gene technologies in medicine

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University of Helsinki, Biomedicum Stem Cell Center &
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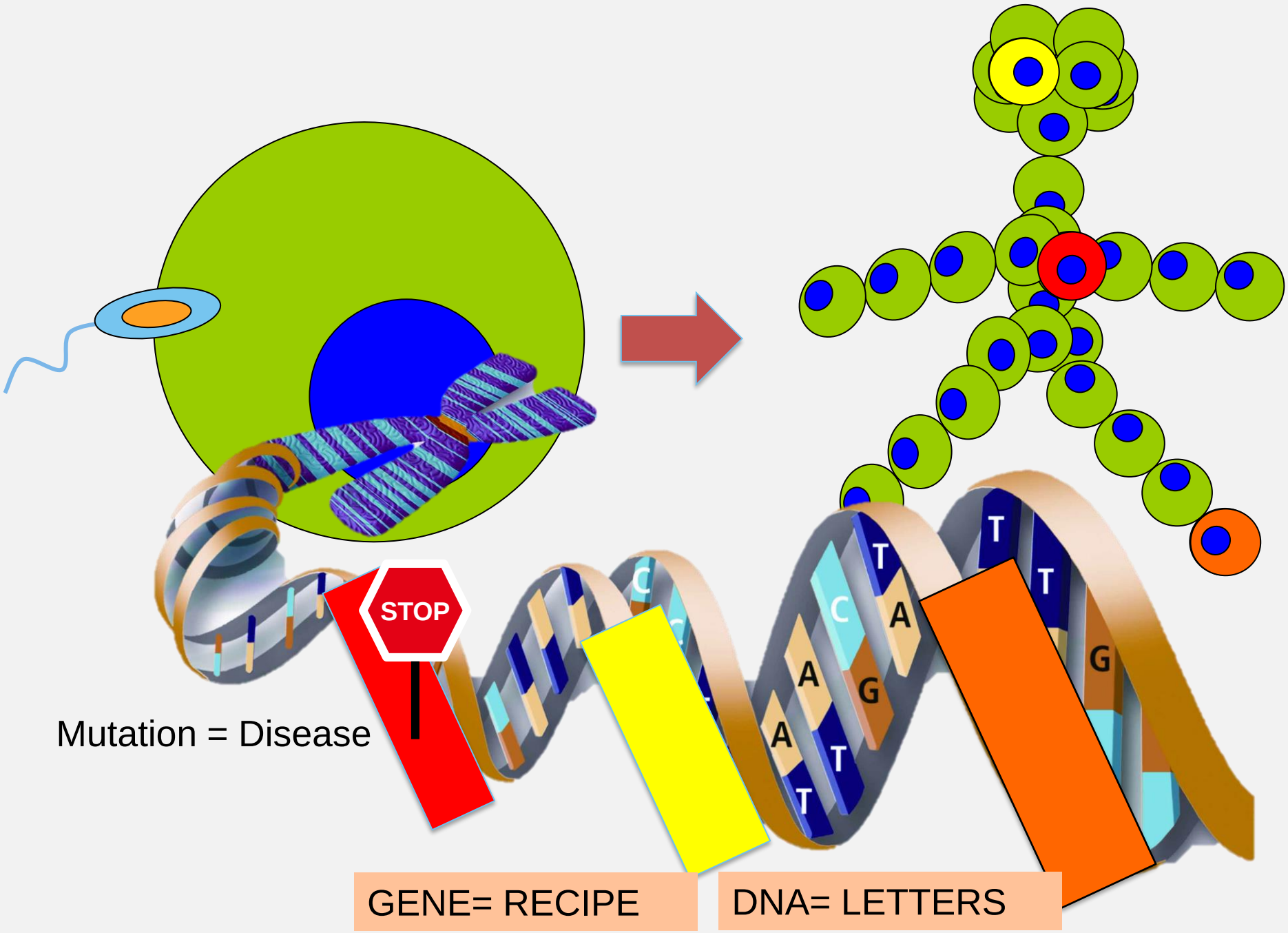

STOP
Mutation = Disease
GENE= RECIPE
DNA= LETTERS

Genetic diseases

Between 1901-2018
- >6000 genetic disorders

Often rare $1:10^4$-10^6
- 400 million patients globally

Annual cost > 50 billion USD

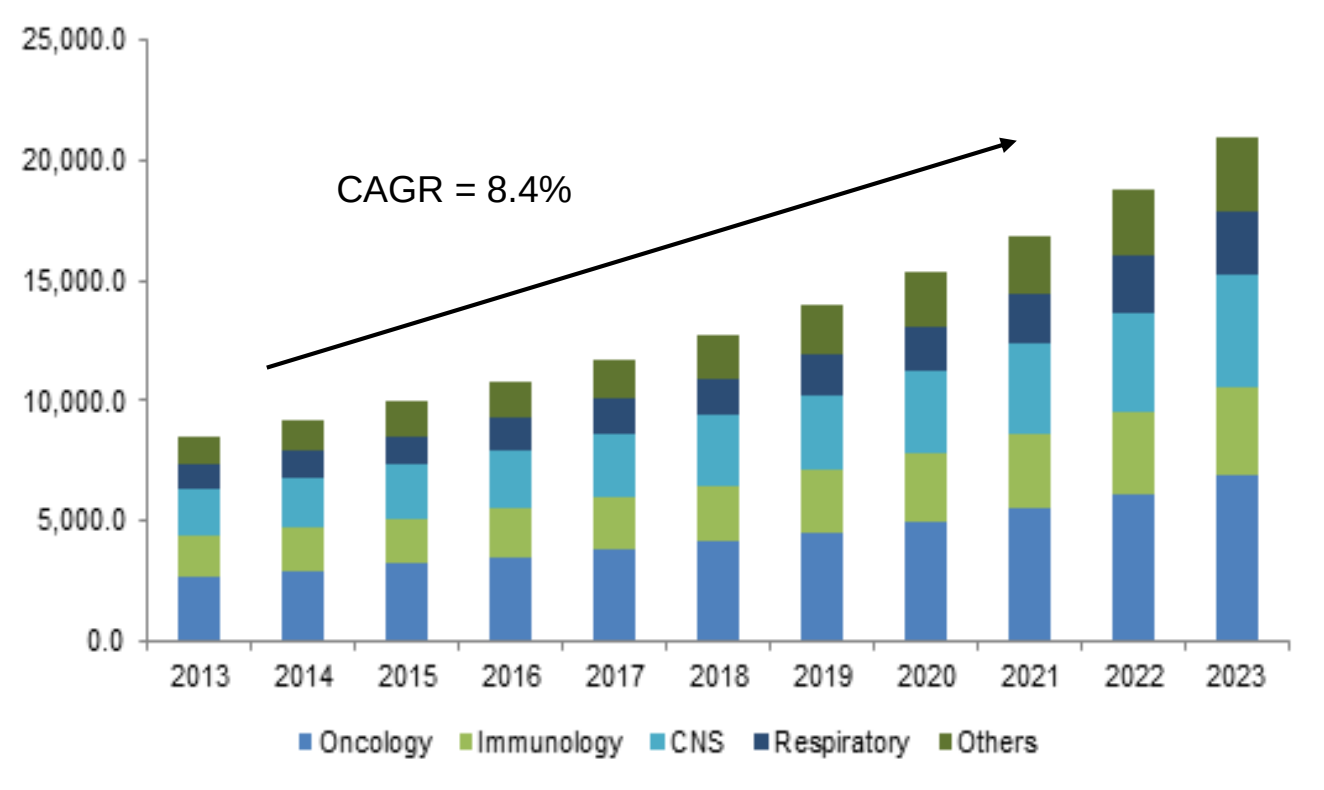
Special Finnish disease inheritance
- 36 monogenic diseases



Alkaptonuria
(black bone disease)

Image:wikipedia

Precision Medicine market in Europe



Europe precision medicine market size
2013 - 2023 (USD Million)

Expected market is $200 M in Finland (2023)

CRISPR-Cas9 technology

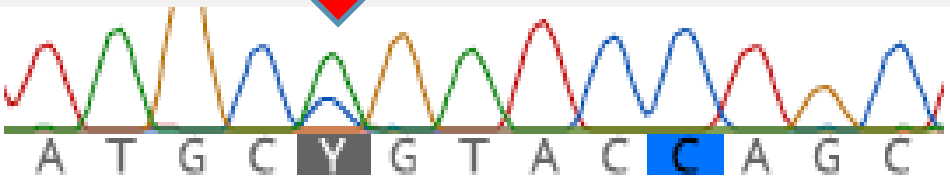


CRISPR-Cas9 technology

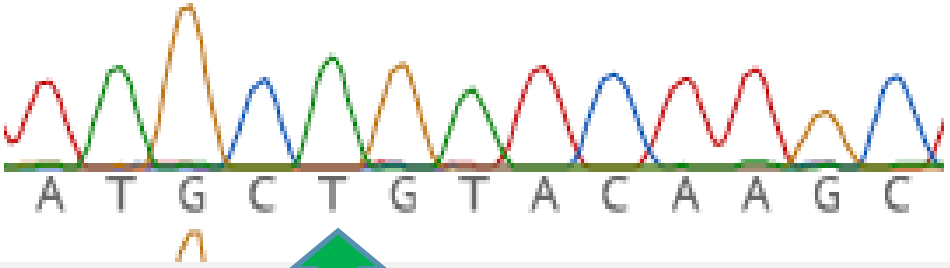
Genetic correction of a patient mutation

MUTATION

Patient-iPS HEL71.4
Heterozygous mutation



Corrected clone F2



CORRECTED

Balboa et al. 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Gene Editing of *CCR5* in Autologous CD4 T Cells of Persons Infected with HIV

Pablo Tebas, M.D., David Stein, M.D., Winson W. Tang, M.D., Ian Frank, M.D., Shelley Q. Wang, M.D., Gary Lee, Ph.D., S. Kaye Spratt, Ph.D., Richard T. Surosky, Ph.D., Martin A. Giedlin, Ph.D., Geoff Nichol, M.D., Michael C. Holmes, Ph.D., Philip D. Gregory, Ph.D., Dale G. Ando, M.D., Michael Kalos, Ph.D., Ronald G. Collman, M.D., Gwendolyn Binder-Scholl, Ph.D., Gabriela Plesa, M.D., Ph.D., Wei-Ting Hwang, Ph.D., Bruce L. Levine, Ph.D., and Carl H. June, M.D.

N Engl J Med 2014; 370:901-910 | March 6, 2014 | DOI: 10.1056/NEJMoa1300662

First-in-man CRISPR trial

PD-1 knock-out immune cells injected into patient with advanced lung cancer



NATURE | NEWS

CRISPR gene-editing tested in a person for the first time

The move by Chinese scientists could spark a biomedical duel between China and the United States.

David Cyranoski

15 November 2016

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First in vivo gene editing in human
(ZFN & Hunter sdr)

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513



Brian Madeux, who has Hunter syndrome, has received a treatment aimed at editing the genome of his liver cells.

AP Photo/Eric Risberg

A human has been injected with gene-editing tools to cure his disabling disease. Here's what you need to know

By Jocelyn Kaiser | Nov. 15, 2017 , 6:00 PM

nature International weekly journal of science

NATURE | ARTICLE

Correction of a pathogenic gene mutation in human embryos

Hong Ma, Nuria Marti-Gutierrez, Sang-Wook Park, Jun Wu, Yeonmi Lee, Keiichiro Suzuki, Amy Koski, Dongmei Ji, Tomonari Hayama, Riffat Ahmed, Hayley Darby, Crystal Van Dyken, Ying Li, Eunju Kang, A.-Reum Park, Daesik Kim, Sang-Tae Kim, Jianhui Gong, Ying Gu, Xun Xu, David Battaglia, Sacha A. Krieg, David M. Lee, Diana H. Wu, Don P. Wolf, Stephen B. Heitner, Juan Carlos Izpisua Belmonte, Paula Amato, Jin-Soo Kim, Sanjiv Kaul & Shoukhrat Mitalipov

Show fewer authors

Affiliations | Contributions | Corresponding authors

Nature (2017) | doi:10.1038/nature23305

Received 28 March 2017 | Accepted 27 June 2017 | Published online 02 August 2017

Unanswered questions: societal

- Hospital procedures and logistics
- Regulatory requirements (commercial interests)
- Public opinions and ethics
  - global equality
  - disease treatment vs individual enhancement
  - inherited modifications
  - other species

MAANANTAI **12.3. 2018 16.00** MONDAY

Yliopiston juhlasali/University Great Hall
Fabianinkatu 33



Dr. SHOUKHRAT MITALIPOV:

Gene repair of heritable mutations

YLEISÖLUENTO/ PUBLIC LECTURE

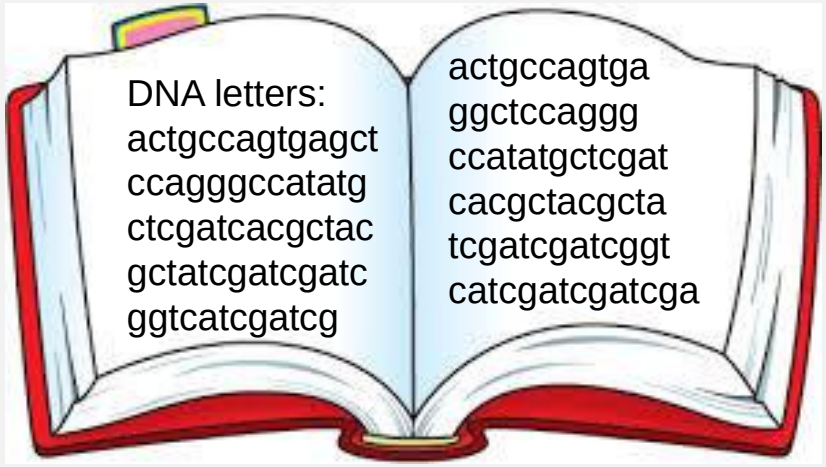
16.00 Introduction by Dr. Kirmo Wartiovaara, chair

16.05 Lecture by **Dr Shoukrat Mitalipov**, Oregon Health Sciences University, USA.

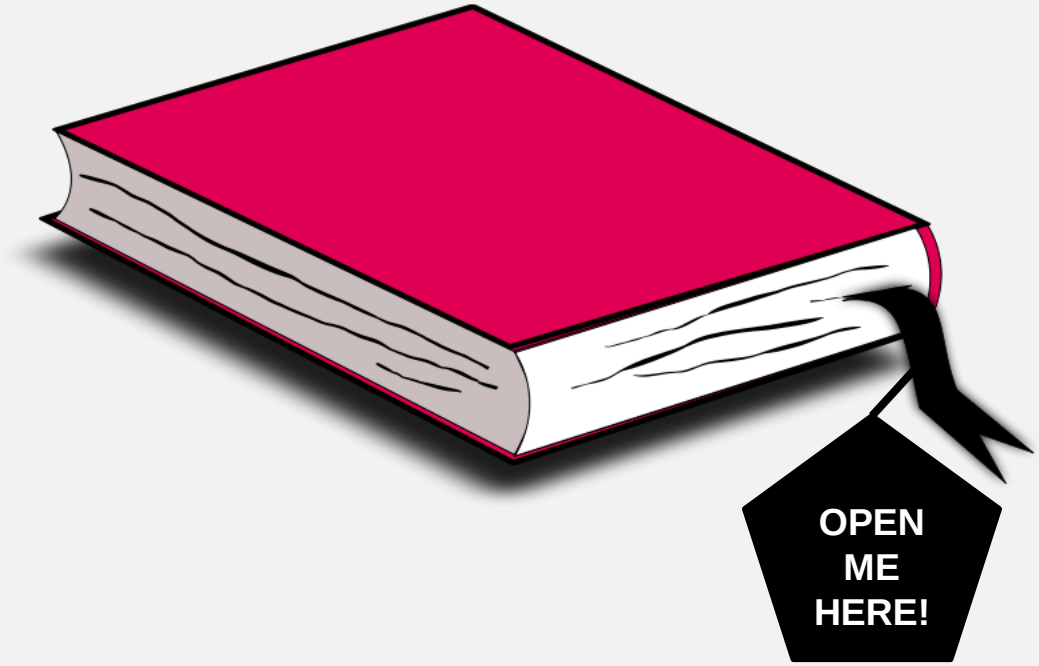
16.50 Commentary remarks by professors Timo Otonkoski and Helena Kääriäinen

17.00-18.00 Public discussion, questions from the audience

Language: **English**, questions translated, if necessary

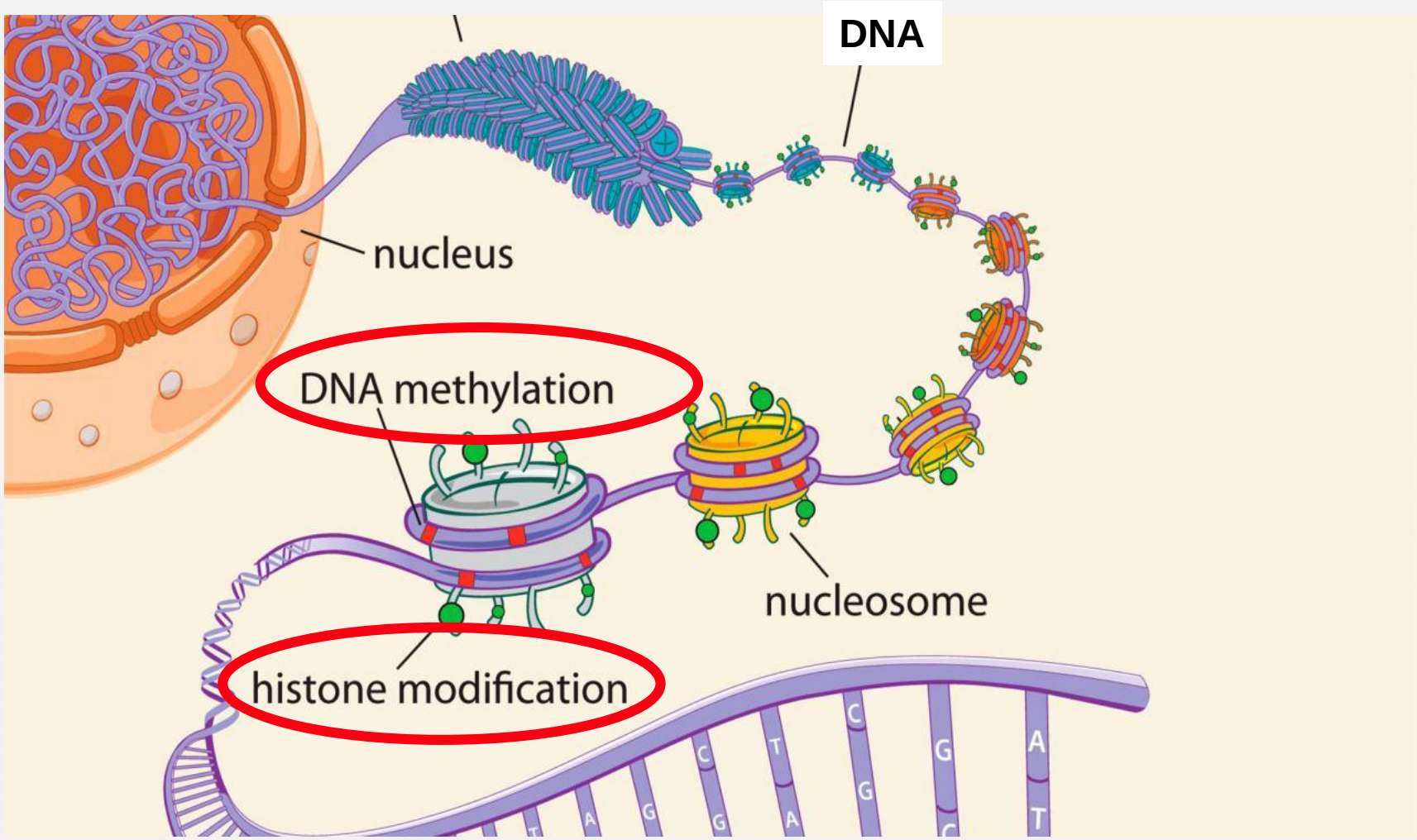


GENETICS:
The recipies



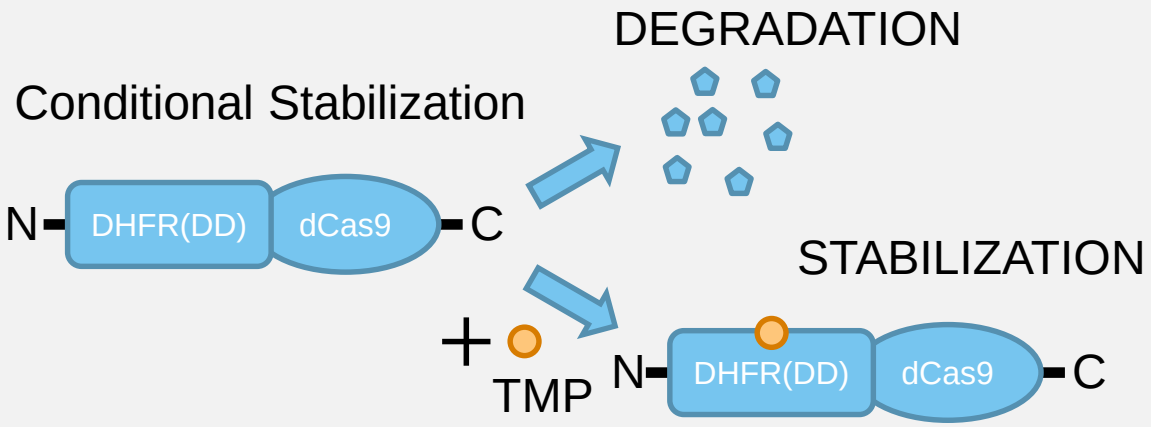
EPIGENETICS:
The bookmarks

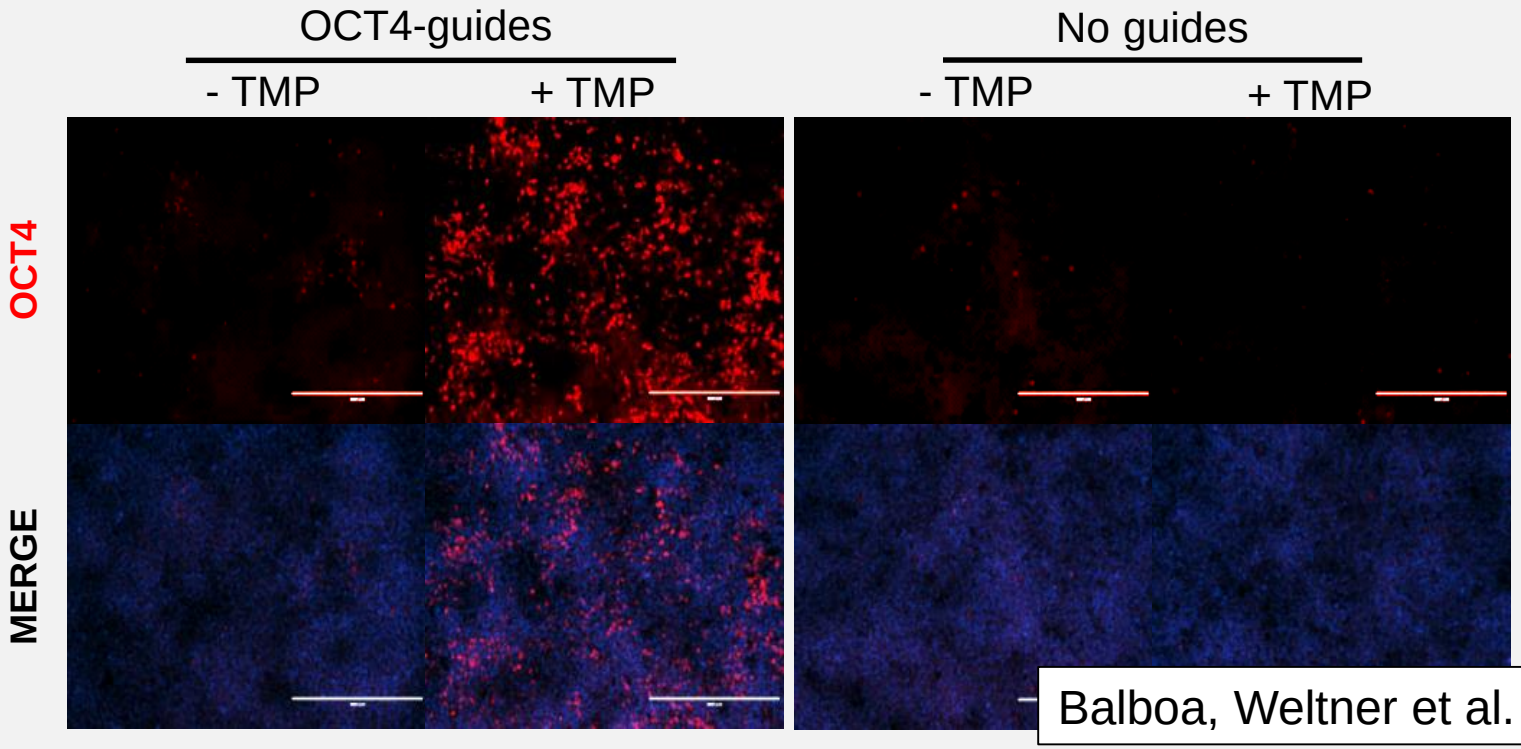
EPIGENETIC MECHANISMS



www.sciencemag.org

Conditional OCT4 activation with destabilized domain (DD)-dCas9VP192





Balboa, Weltner et al. 2015

Clinical trials of epigenetics



A CRISPR design for next-generation antimicrobials.

Chase L Beisel, Ahmed A Gomaa and Rodolphe Barrangou.

Genome Biol. 2014; 15(11): 516.

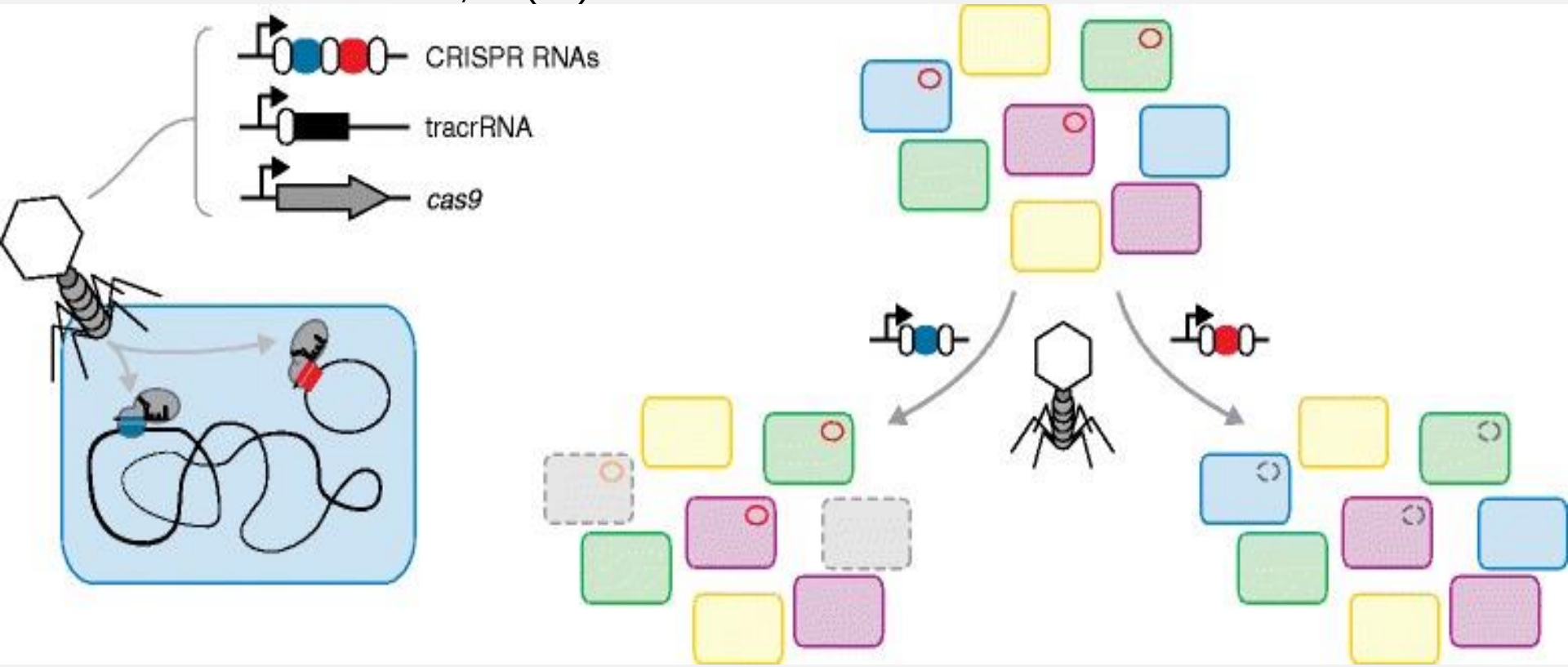


Figure 1. **Delivering CRISPR-Cas9 for targeted killing and plasmid removal.** Left: phages are engineered to encode the Cas9 nuclease, a trans-activating crRNA (tracrRNA) and an array of plasmid-targeting or genome-targeting CRISPR RNAs. The CRISPR RNAs are designed to target unique sequences in the bacterial chromosome or in harbored plasmids. Right: injection of the phage DNA into a mixed population of bacteria leads to removal (here depicted with broken lines) of targeted strains or plasmids without impacting the rest of the population. With further development, this strategy has the potential to treat multidrug-resistant infections without impacting beneficial microbes, to remove contaminating microbes from industrial fermentations and to provide further insights into microbial communities

DNA detection with CRISPR-Cas

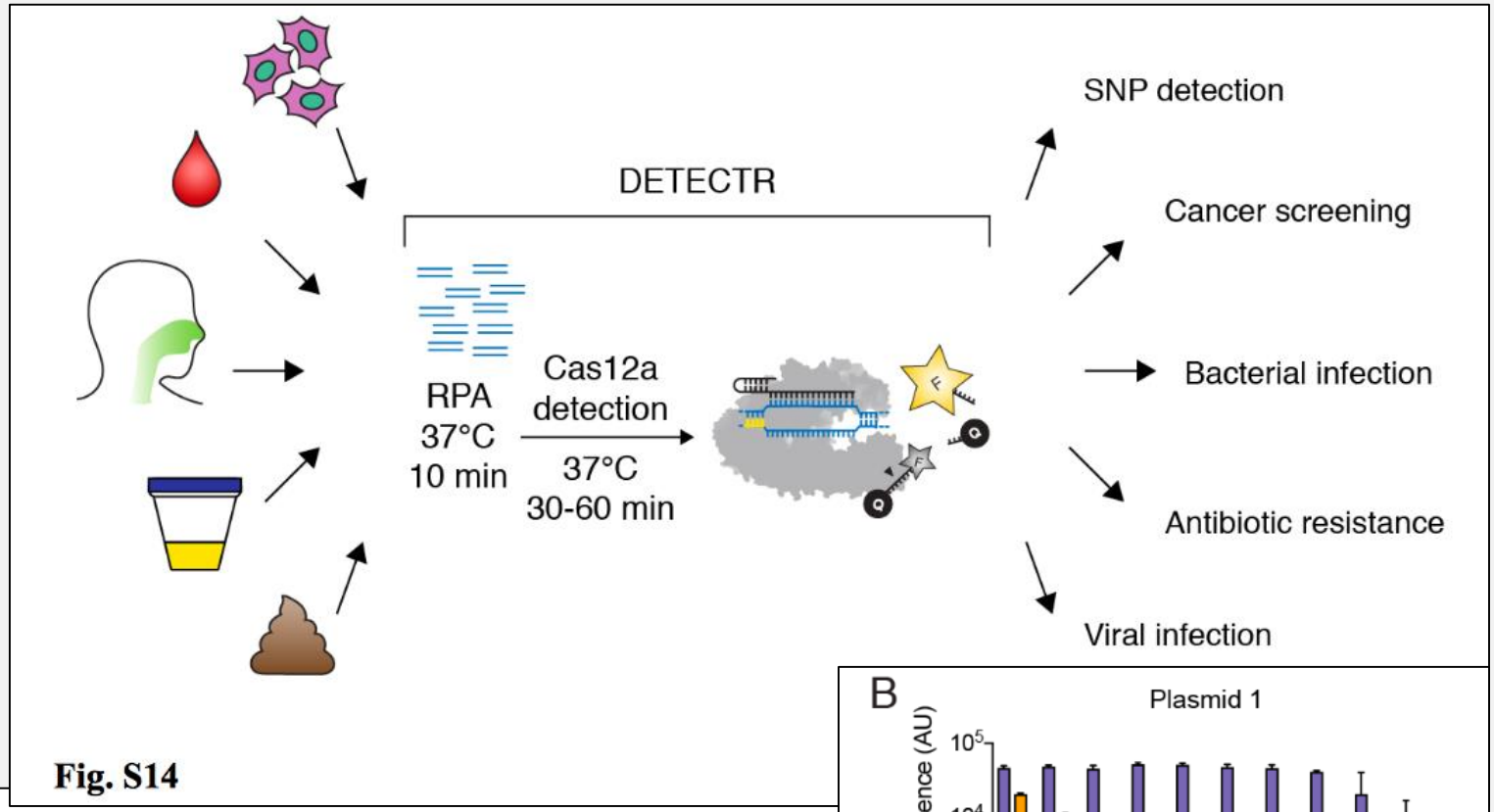


Fig. S14

Science

REPORTS

Cite as: J. S. Chen *et al.*, *Science* 10.1126/science.aar6245 (2018).

CRISPR-Cas12a target binding unleashes indiscriminate single-stranded DNase activity

Janice S. Chen,[1*] Enbo Ma,[1*] Lucas B. Harrington,[1*] Maria Da Costa,[2] Xinran Tian,[3] Joel M. Palefsky,[2] Jennifer A. Doudna[1,3,4,5,6†]

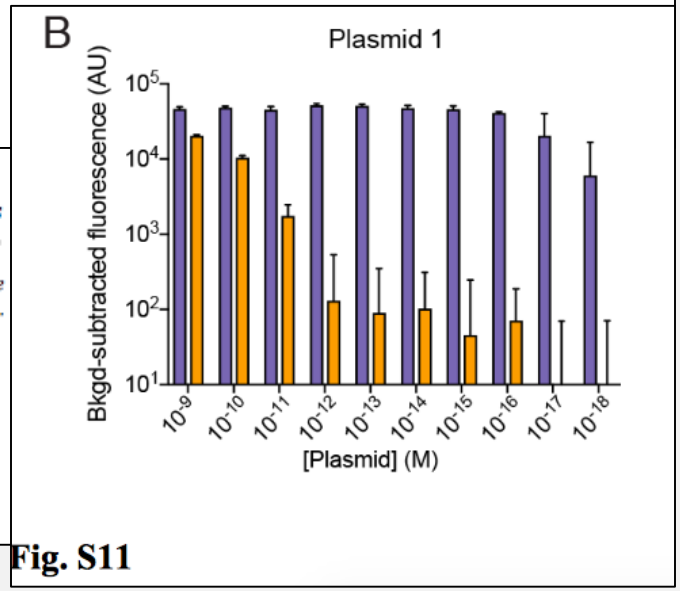


Fig. S11



Financial supporters: Academy of Finland, University of Helsinki, Foundation for Pediatric Research, Helsinki University Hospital

Toivomuslista Suomelle

- CRISPR – ohjeistus (Suomi-EU)!
- Lääkäreiden tutkimuksen mahdollistaminen

- Koulutuksen arvostus puheissa ja teoissa
- Tiedeministeriö

Lisätietoa keskustelua varten:

EASAC policy report 31

March 2017

ISBN: 978-3-8047-3727-3

This report can be found at
www.easac.eu

European Academies
easac
Science Advisory Council

Science Advice for the Benefit of Europe

Genome editing: scientific opportunities, public interests and policy options in the European Union



HUMAN GENOME EDITING
Science, Ethics, and Governance

Committee on Human Gene Editing:
Scientific, Medical, and Ethical Considerations

A Report of
NATIONAL ACADEMY OF SCIENCES *AND*
NATIONAL ACADEMY OF MEDICINE

THE NATIONAL ACADEMIES PRESS
Washington, DC
www.nap.edu

Feb 14, 2017

In light of the technical and social concerns involved, the committee concluded that germline genome-editing research trials might be permitted, but only following much more research aimed at meeting existing risk/benefit standards for authorizing clinical trials and even then, only for compelling reasons and under strict oversight. It would be essential for this research to be approached with caution, and for it to proceed with broad public input.

nature International weekly journal of science

NATURE | NEWS FEATURE

Welcome to the CRISPR zoo

Birds and bees are just the beginning for a burgeoning technology.

Sara Reardon

09 March 2016

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