Braucht man heute noch Zwillingsforschung?

Olaf Riess
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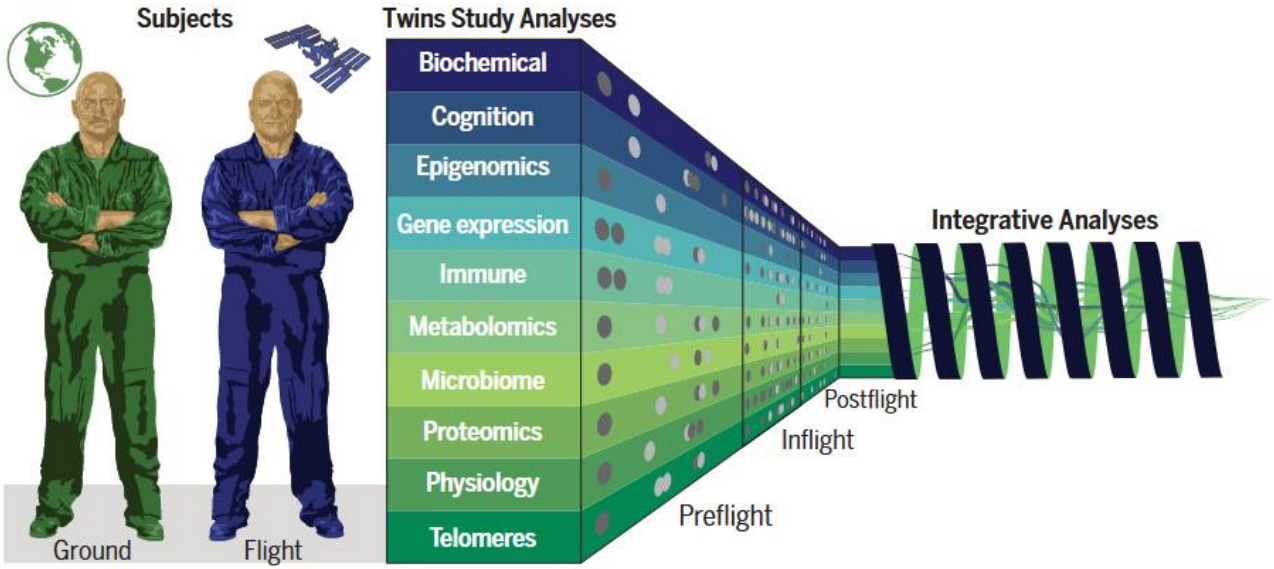
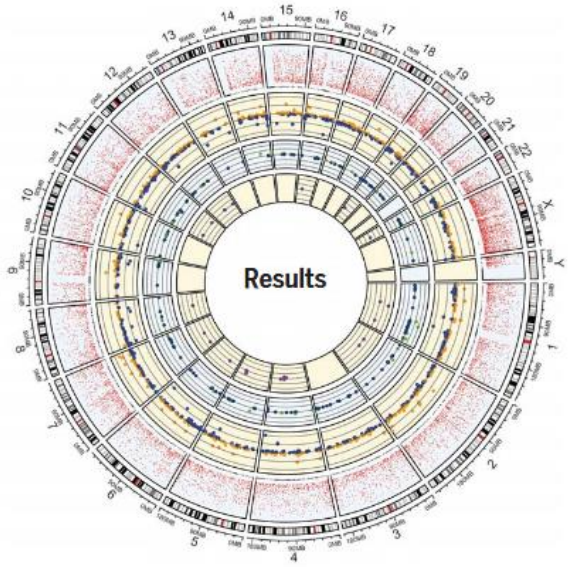
NASA‘s Twin Study

340 days on ISS

Pre-flight In-flight Post-flight





Garrett-Bakelman et al. Science 364:144 (2019)

NASA‘s Twin Study

Total study duration 25 month

Pre-flight In-flight Post-flight

Telomere length => telomere length increased during flight (14.5%),
shortened immediately after return to earth
Transcriptome => some changes remain even after 6 month on earth
Genome => increased DNA damage from chromosomal inversions
Epigenome
Immune system => First vaccination in flight (influenca) !
Cardiovascular
Metabolome
Gut microbiome
Physiology
Vision
Cognition

Health and safety in long term space missions

Garrett-Bakelman et al. Science 364:144 (2019)

Understanding Genetic and Environmental Influences Using Twin Studies

Monozygotic Twins

100% genes
100% home environment

Dizygotic Twins

50% genes
100% home environment

We are a combination of our genes and environment.

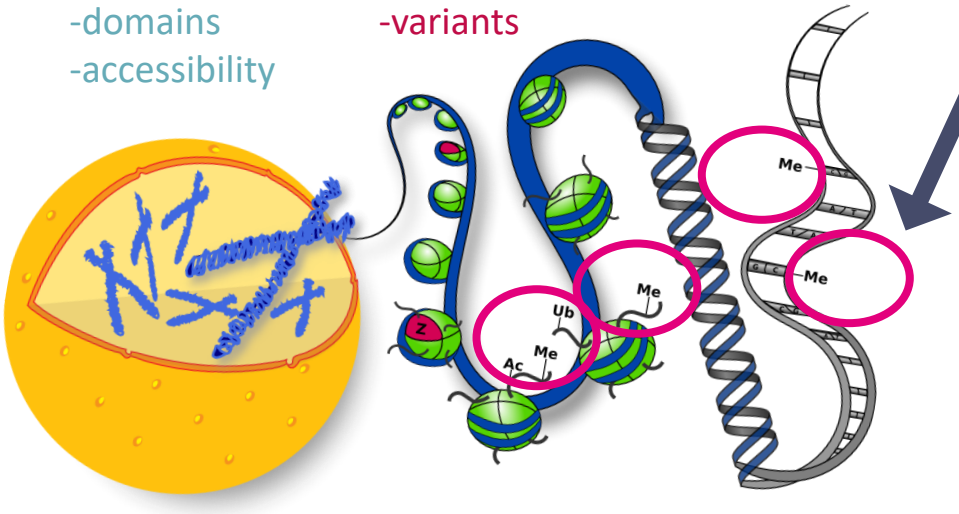
Epigenome Profiling using NGS

The human genome contains about **28 Mio CpG** sites that can be methylated and potentially affect gene expression.

Chromatin
-structure
-domains
-accessibility

Histone
-modifications
-variants

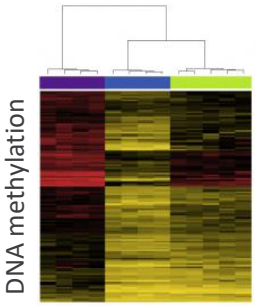
DNA
-modifications



3C, 4C, 5C, Hi-C, ChIA-PET, DNAse-seq, FAIRE-seq, ATAC-seq	ChIP-seq Mnase-seq	WGBS, RRBS, MeDIP-seq, Methyl-seq

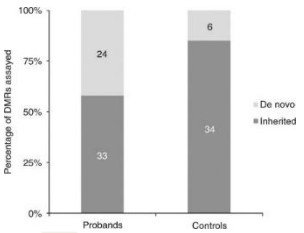
Rare Diseases

Episignatures



Erfan Aref-Eshghi *et al* 2020

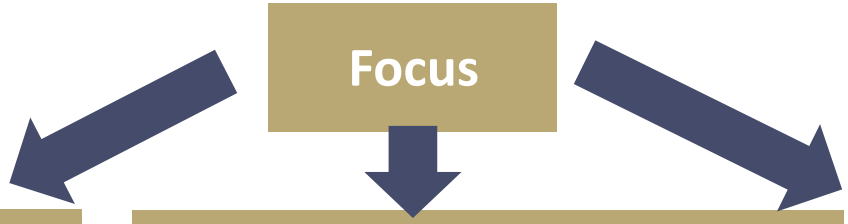
Epivariants



Mafalda Barbosa *et al* 2018

Universitätsklinikum Tübingen

Genetic Twin Research across the world



Monogenic diseases

Discordant twins

Polygenic diseases and Health

Discordant twins
Life style and nutrition
Biomarker development

Biology

Genome structure
Epigenome
Transcriptome

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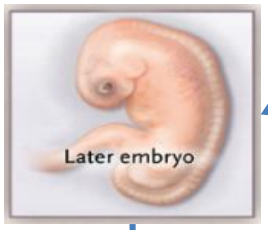
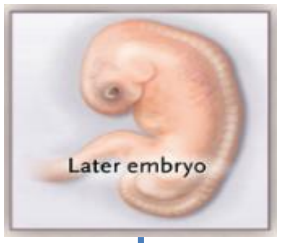
15.07.2021

Diskordante monozygote Zwillinge
„Next-Level-Mosaikerkrankung“

Keimbahnmutationen / vererbte Merkmale
=
identische Zwillinge





Prämorula-Mutationen

oder

somatische Mutationen

=

diskordante Zwillinge

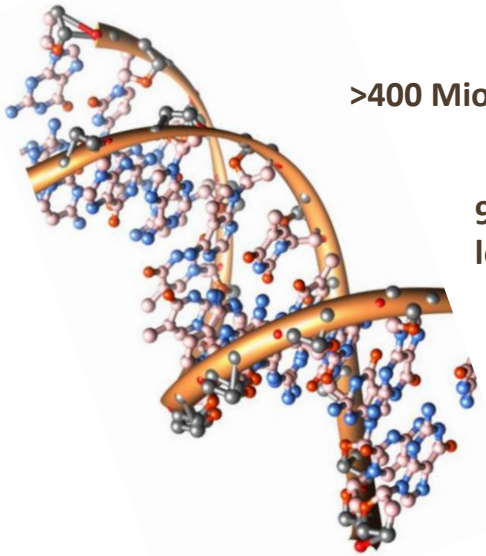
Determining the incidence of a disease in twins helps delineate whether there are genetic and environmental components

Both genetic and environmental factors important

Disease	*Concordance*	
	Identical (MZ)	*Non-identical (DZ)*
Cleft lip and palate	38%	8%
Rheumatoid arthritis	34%	7%
Asthma	47%	24%
Coronary artery disease	19%	9%
Diabetes mellitus	56%	11%

Complexity of analysing genomes in the clinical context

TOPMed study (Trans-Omics for Precision Medicine)



53,831 Genomes analysed

>400 Mio variants

97% of the variants less than 1%

53% present in only 1 individual

-> 4,6 Mio protein-coding variants
Total 230,000 putative loss of function variants in 18.493 genes
-> 104,000 frameshift variants
-> 97,000 putative splice and truncation variants

2.5 unique pLOF per individual

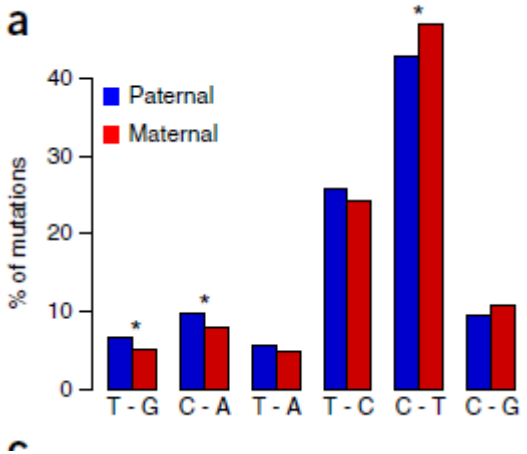
Additional read out needed !

https://www.shutterstock.com/de/image-illustration/organic-chemistry-model-dna-molecule-illustration-93597241?id=93597241

Nature Vol.590, 2021

nature genetics

45 – 60 *de novo* mutations per child / genome



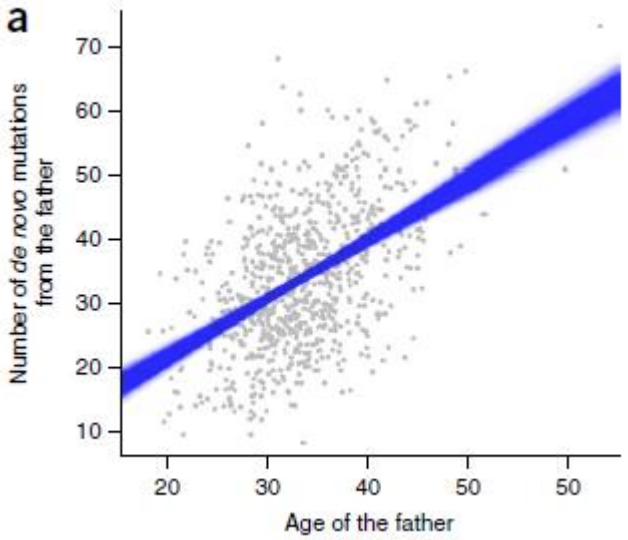
Parent-of-origin-specific signatures of *de novo* mutations

Jakob M Goldmann[1,10], Wendy S W Wong[2,10], Michele Pinelli[3], Terry Farrah[4], Dale Bodian[2], Anna B Stittrich[4], Gustavo Glusman[4], Lisenka E L M Vissers[5], Alexander Hoischen[5], Jared C Roach[4], Joseph G Vockley[2,6], Joris A Veltman[5,7], Benjamin D Solomon[2,8,9], Christian Gilissen[5,11] & John E Niederhuber[2,9,11]

Table 1 Cohort description

Birth constellation	No. births	No. children	No. sequenced samp
Singletons	731	731	2,193
Dizygotic twins	35	70	140
Monozygotic twins	14	28	56
Triplet	1	3	5
Total	781	832	2,394

The cohort consists of 731 trios, 49 quartets, and one quintet, resulting in a total of 832 children.

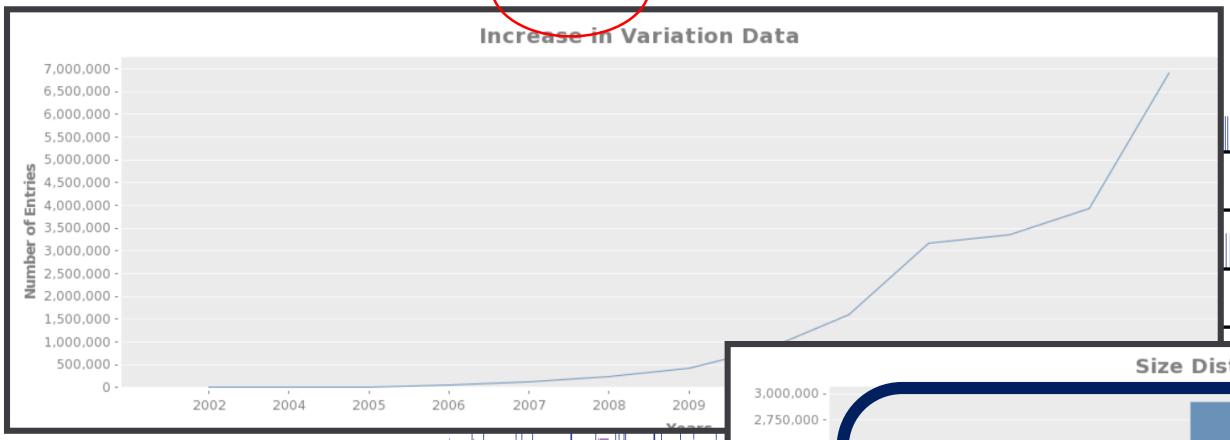


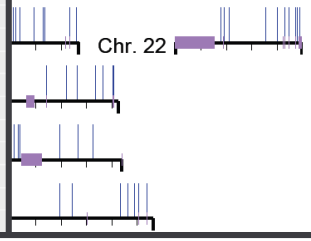
Characterization of missing human genome sequences and copy-number polymorphic insertions

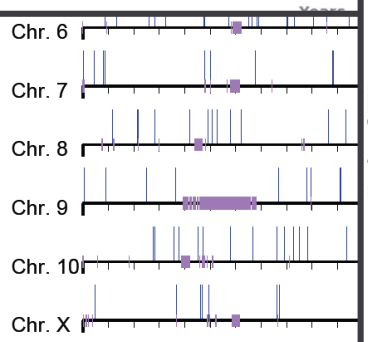
Jeffrey M Kidd[1], Nick Sampas[2], Francesca Antonacci[1], Tina Graves[3], Robert Fulton[3], Hillary S Hayden[1], Can Alkan[1], Maika Malig[1], Mario Ventura[4], Giuliana Giannuzzi[4], Joelle Kallicki[3], Paige Anderson[2], Anya Tsalenko[2], N Alice Yamada[2], Peter Tsang[2], Rajinder Kaul[1], Richard K Wilson[3], Laurakay Bruhn[2] & Evan E Eichler[1,5]

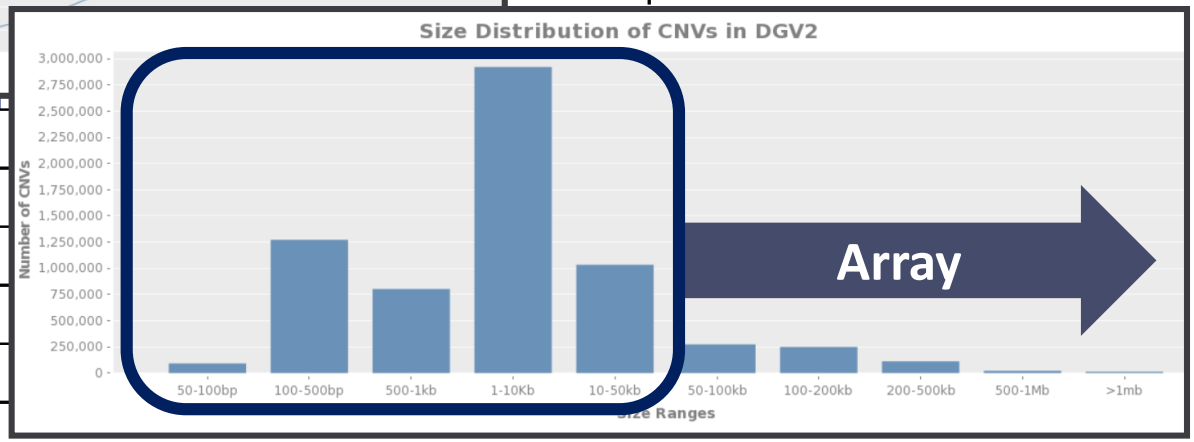
NATURE METHODS | VOL.7 NO.5 | MAY 2010

2,363 new insertion sequences corresponding to **720** genomic loci.









Array

Treatment studies in rare diseases

Han *et al. Orphanet Journal of Rare Diseases* (2019) 14:232
https://doi.org/10.1186/s13023-019-1216-0

Orphanet Journal of Rare Diseases

RESEARCH Open Access

A placebo-controlled trial of folic acid and betaine in identical syndrome

Julia Han[1], Terry Jo Bichell[2], Stephanie Golde
Lynne M. Bird[7,8] and Virginia Kimonis[1,2*]

Ismaylova et al. *Translational Psychiatry* (2018)8:147
DOI 10.1038/s41398-018-0195-6

Translational Psychiatry

ARTICLE Open Access

Serotonin transporter promoter methylation in peripheral cells and neural responses to negative stimuli: A study of adolescent monozygotic twins

Elmira Ismaylova[1,2], Melissa L. Lévesque[1,2], Florence B. Pomares[1,3], Moshe Szyf[4], Zsofia Nemoda[4], Cherine Fahim[1], Frank Vitaro[1,5], Mara Brendgen[1,6], Ginette Dionne[7], Michel Boivin[7,8], Richard E. Tremblay[1,9,10] and Linda Booij[1,2,3]

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Lessons learned from twins

Rare and common diseases
Control of one twin in biomarker and even for treatment studies
Variability of the human organism
- to respond to environment
- and how the organism responds
Human health and aging

New „Omics“ technologies lead to a Renaissance of twin research
From phenotype description to in depth Multi-Omics analysis

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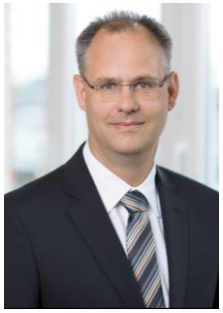

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T. Haack
Molecular
Diagnostics

ZSE TÜBINGEN
Zentrum für Seltene Erkrankungen

Olaf Riess

I declare to receive an explorative grant from Illumina for implementing WGS into clinical care.

https://www.medizin.uni-tuebingen.de/de/das-klinikum/einrichtungen/institute/medizinische-genetik-und-angewandte-genomik

SolveRD

NCCT
NGS Competence Center Tübingen

Institut für
Medizinische Genetik und
Angewandte Genomik

Deutschland
Land der Ideen
Ausgewählter Ort 2011