



# Hvordan screener man børn for **kræft**?

**Ulrik Kristoffer Stoltze, MD, PhD**  
om PREDiSPOSED projektet

# Klinisk genetik

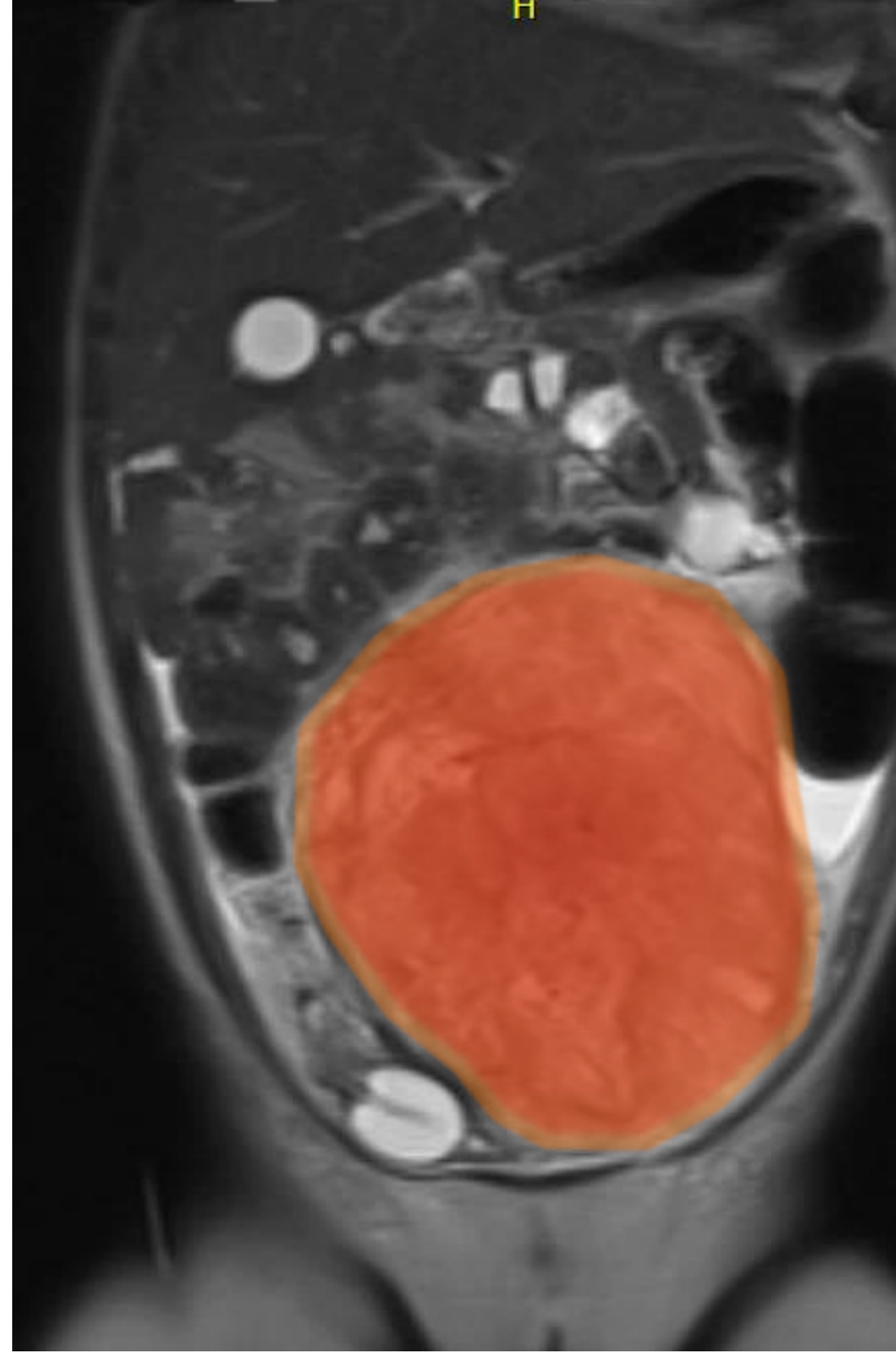
# Klinisk pædiatrisk onkogenetik





# Li-Fraumeni Syndrom

*Symptomer: måneder*







Starter screening

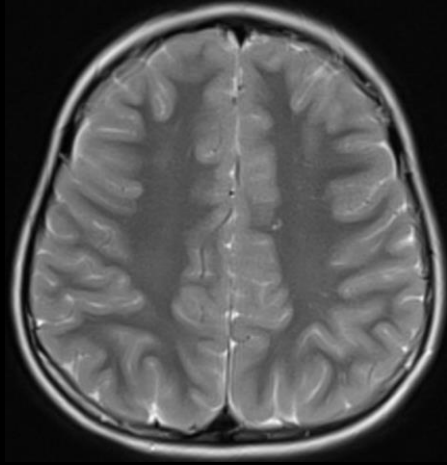
Li-Fraumeni Syndrom



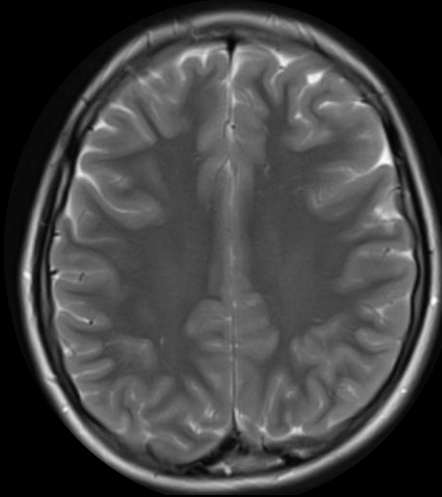


# Helkrops MR skanning

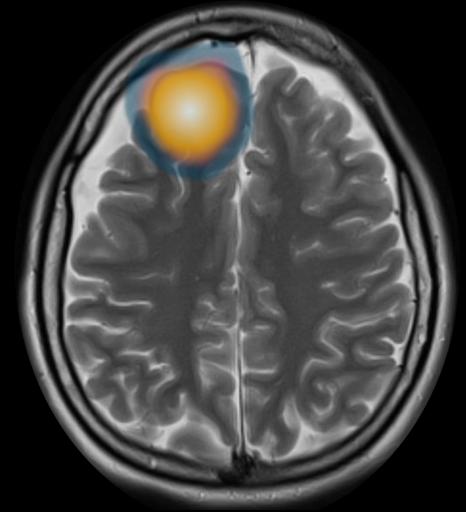
# Baseline Helkrops MR skanning på raske børn



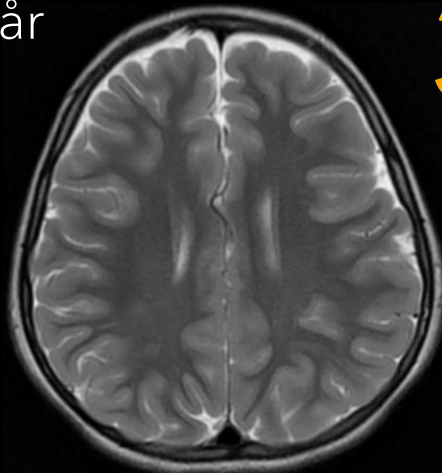
**1** Dreng på 9 år  
*uden fund*



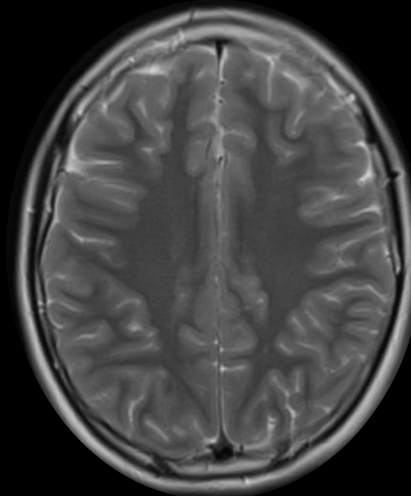
**3** Pige på 12 år  
*uden fund*



**5** Pige på 15 år  
*tumor*

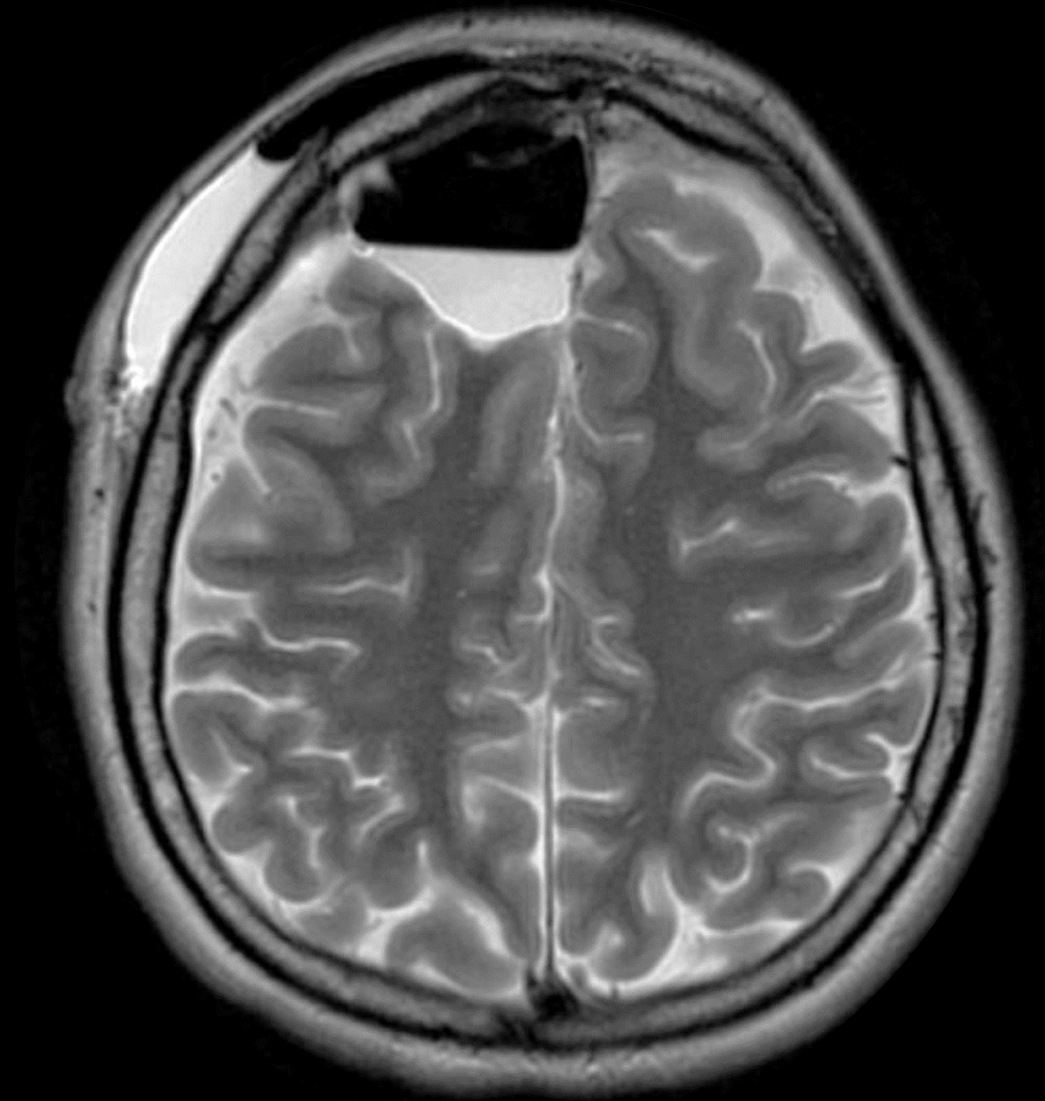


**2** Pige på 8 år  
*uden fund*



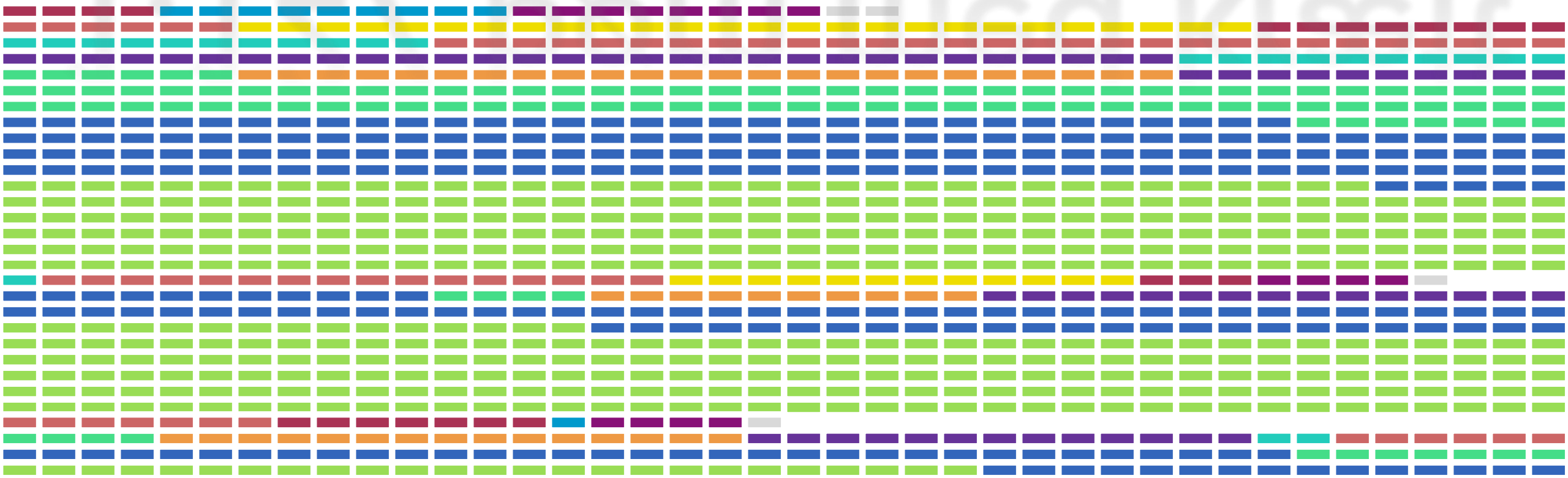
**4** Dreng på 13 år  
*uden fund*

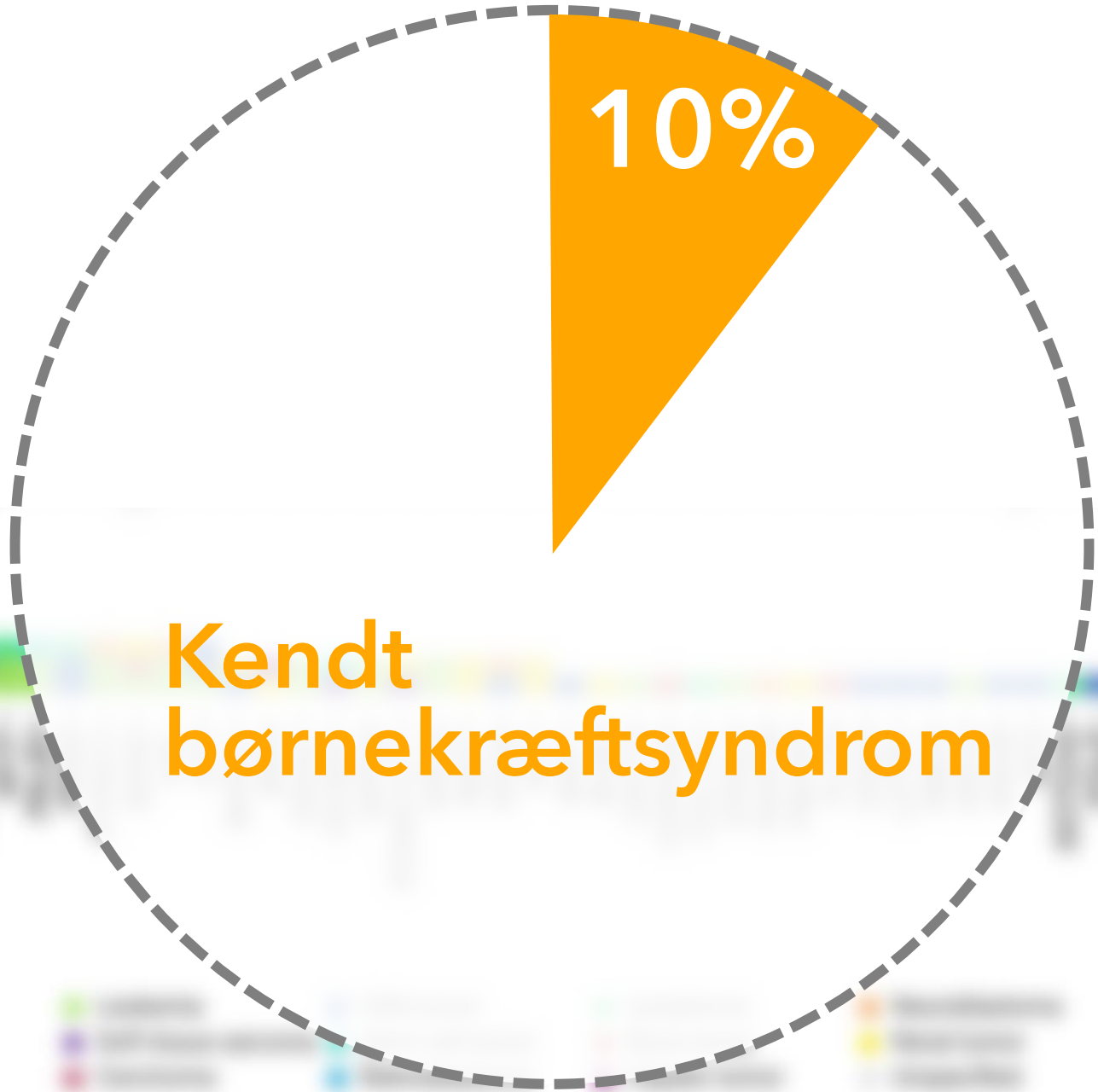
**Patient**  
Sund & rask  
Grad 3 astrocytom  
Operabel





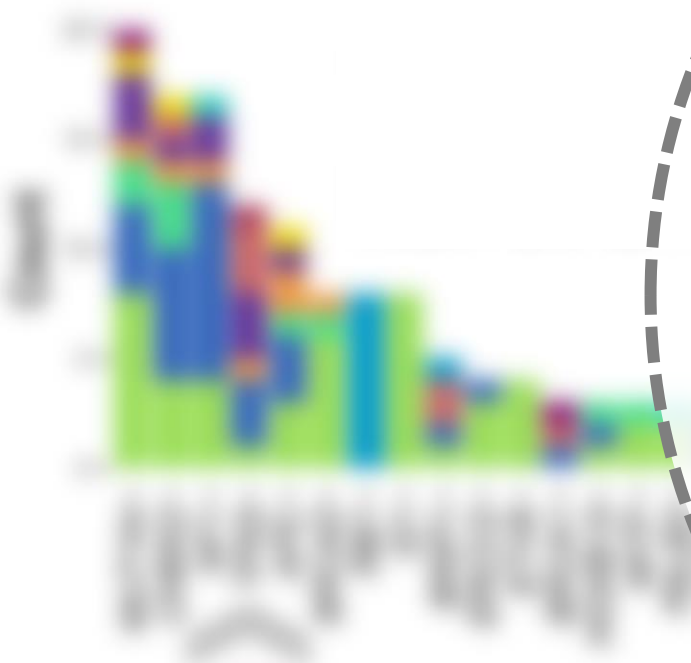
# 1.127 børn med kræft





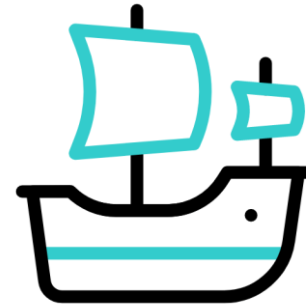
**Kendt  
børnekræftsyndrom**

10%



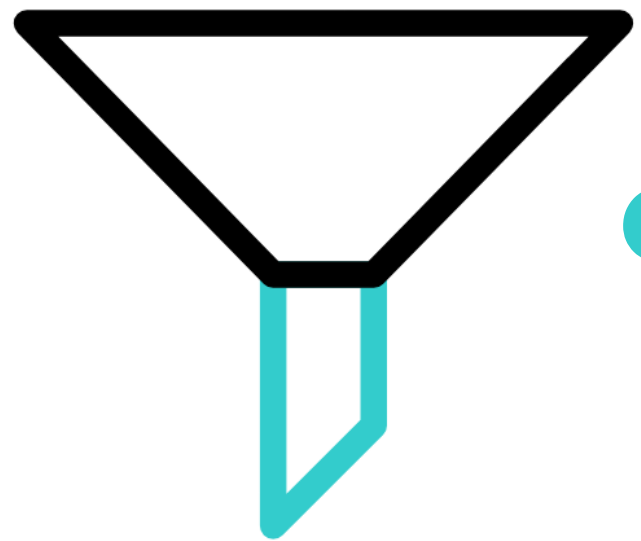


**Bombefly &  
Børnekræft**



**Kaptajn Grant  
Problemet**

4.000.000

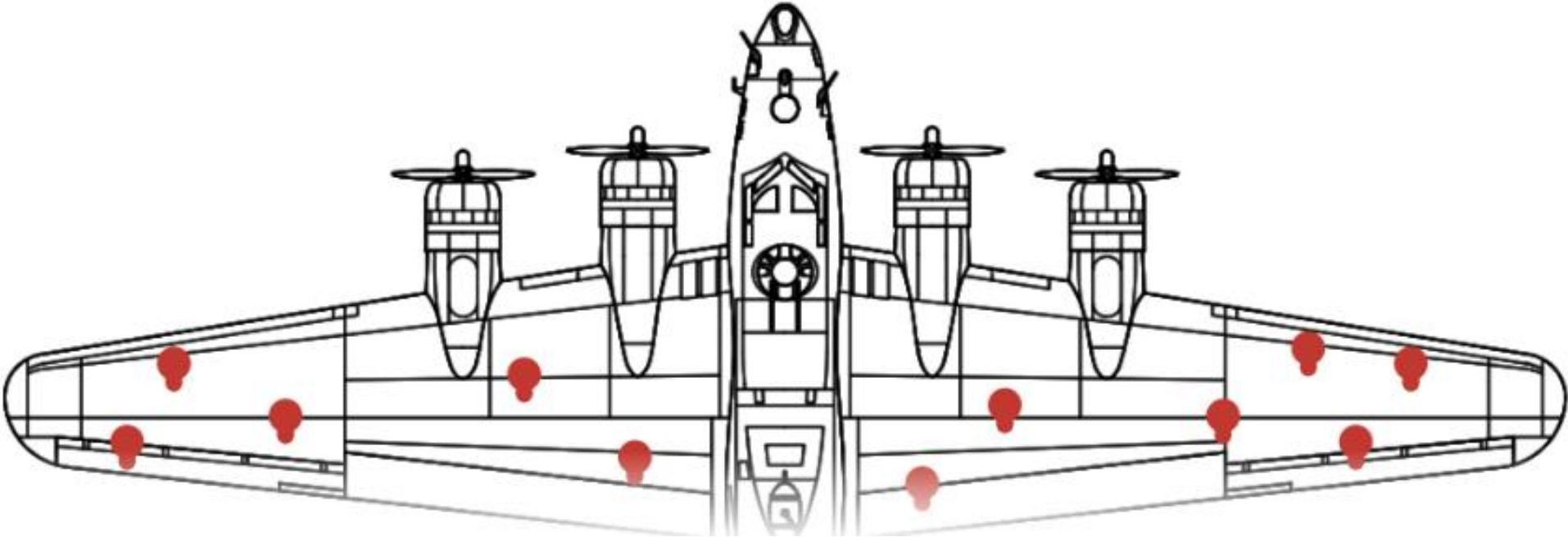


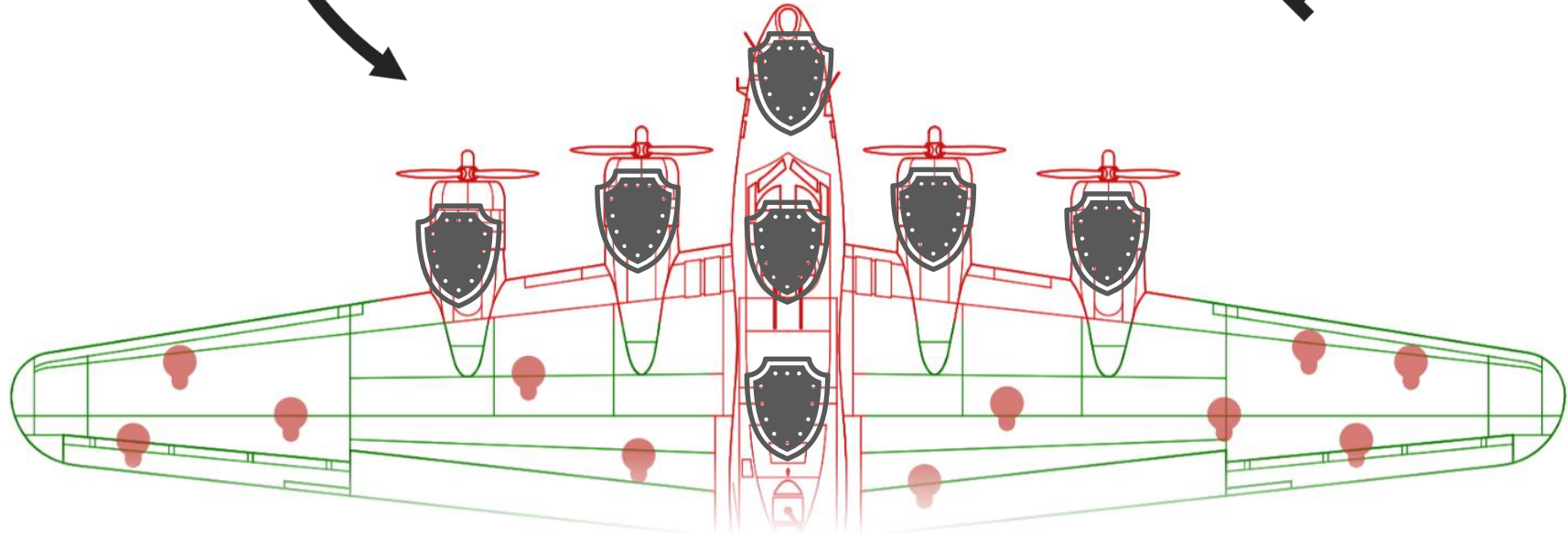
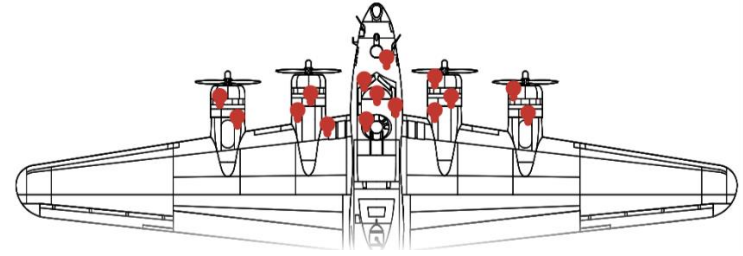
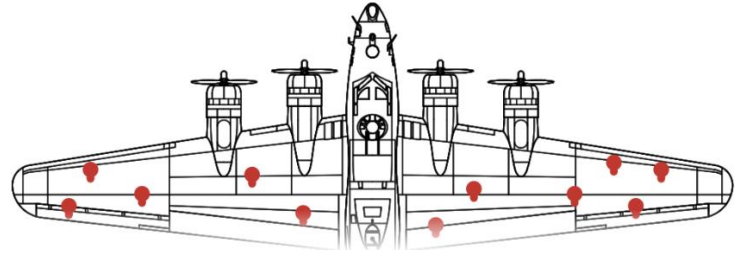
99.999999%

20

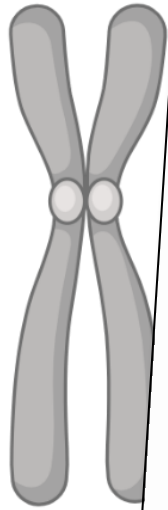
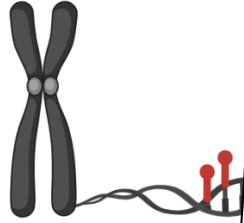


99.99999%









Article


<https://doi.org/10.1038/s41467-024-45975-9>








# The evolutionary impact of childhood cancer on the human gene pool

Received: 16 March 2023

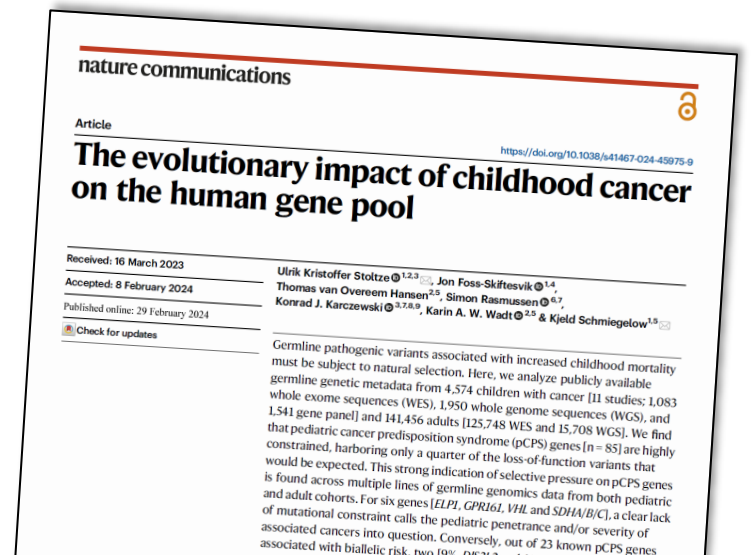
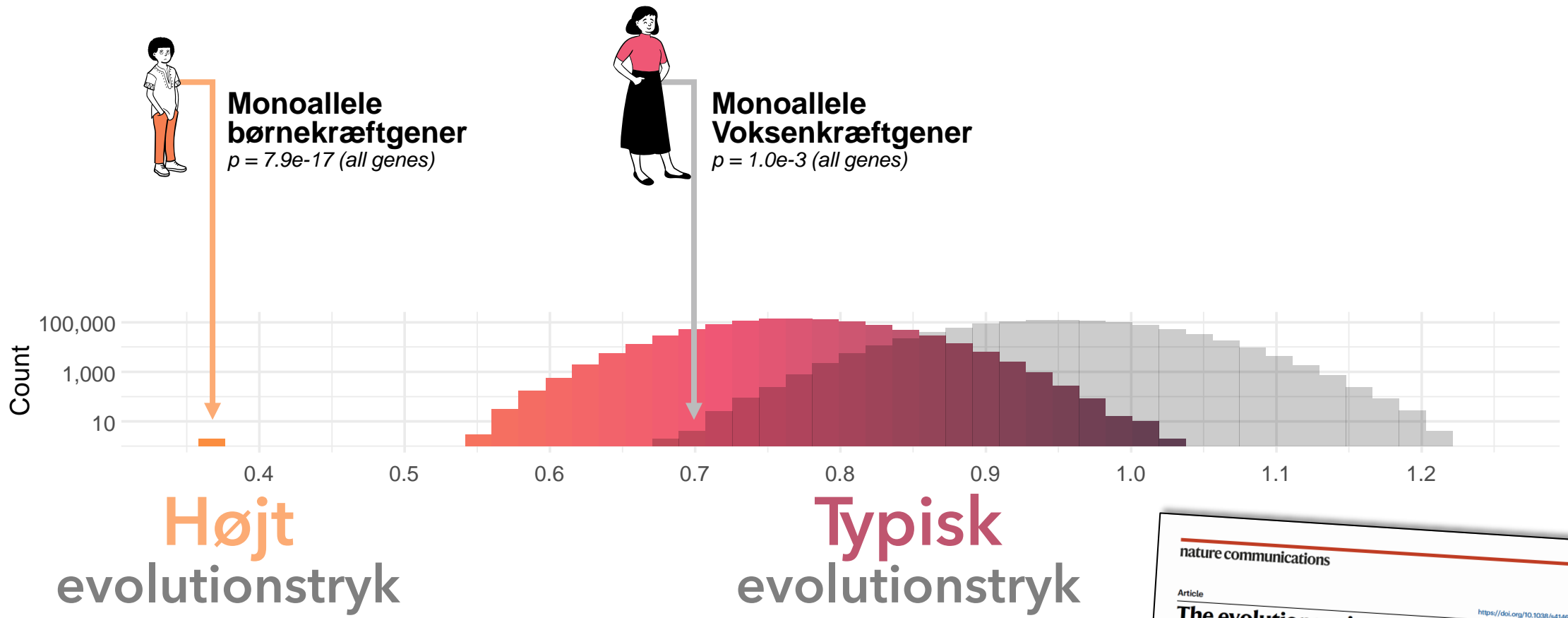
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 Check for updates

Ulrik Kristoffer Stoltze <sup>1,2,3</sup> , Jon Foss-Skiftesvik <sup>1,4</sup>,  
Thomas van Overeem Hansen <sup>2,5</sup>, Simon Rasmussen <sup>6,7</sup>,  
Konrad J. Karczewski <sup>3,7,8,9</sup>, Karin A. W. Wadt <sup>2,5</sup> & Kjeld Schmiegelow <sup>1,5</sup> 

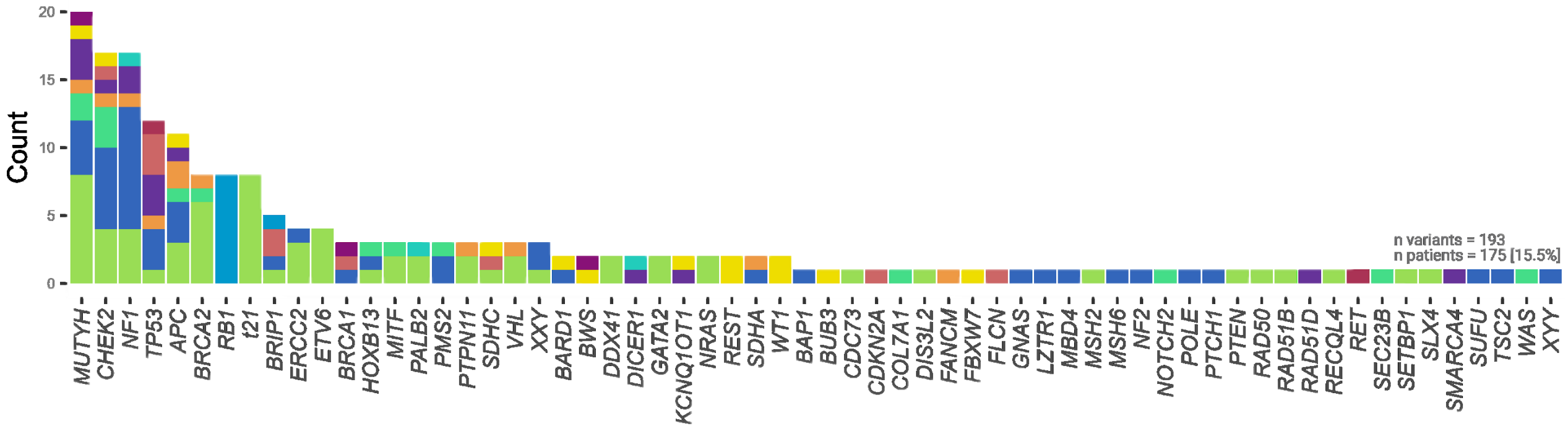
Germline pathogenic variants associated with increased childhood mortality must be subject to natural selection. Here, we analyze publicly available germline genetic metadata from 4,574 children with cancer [11 studies; 1,083 whole exome sequences (WES), 1,950 whole genome sequences (WGS), and 1,541 gene panel] and 141,456 adults [125,748 WES and 15,708 WGS]. We find that pediatric cancer predisposition syndrome (pCPS) genes [ $n = 85$ ] are highly constrained, harboring only a quarter of the loss-of-function variants that would be expected. This strong indication of selective pressure on pCPS genes is found across multiple lines of germline genomics data from both pediatric and adult cohorts. For six genes [*ELPI*, *GPRI61*, *VHL* and *SDHA/B/C*], a clear lack of mutational constraint calls the pediatric penetrance and/or severity of associated cancers into question. Conversely, out of 23 known pCPS genes associated with biallelic risk, two [9%, *DIS3L2* and *MSH2*] show significant constraint, indicating that they may monoallelically increase childhood cancer risk. In summary, we show that population genetic data provide empirical evidence that heritable childhood cancer leads to natural selection powerful enough to have significantly impacted the present-day gene pool.



99.99999%

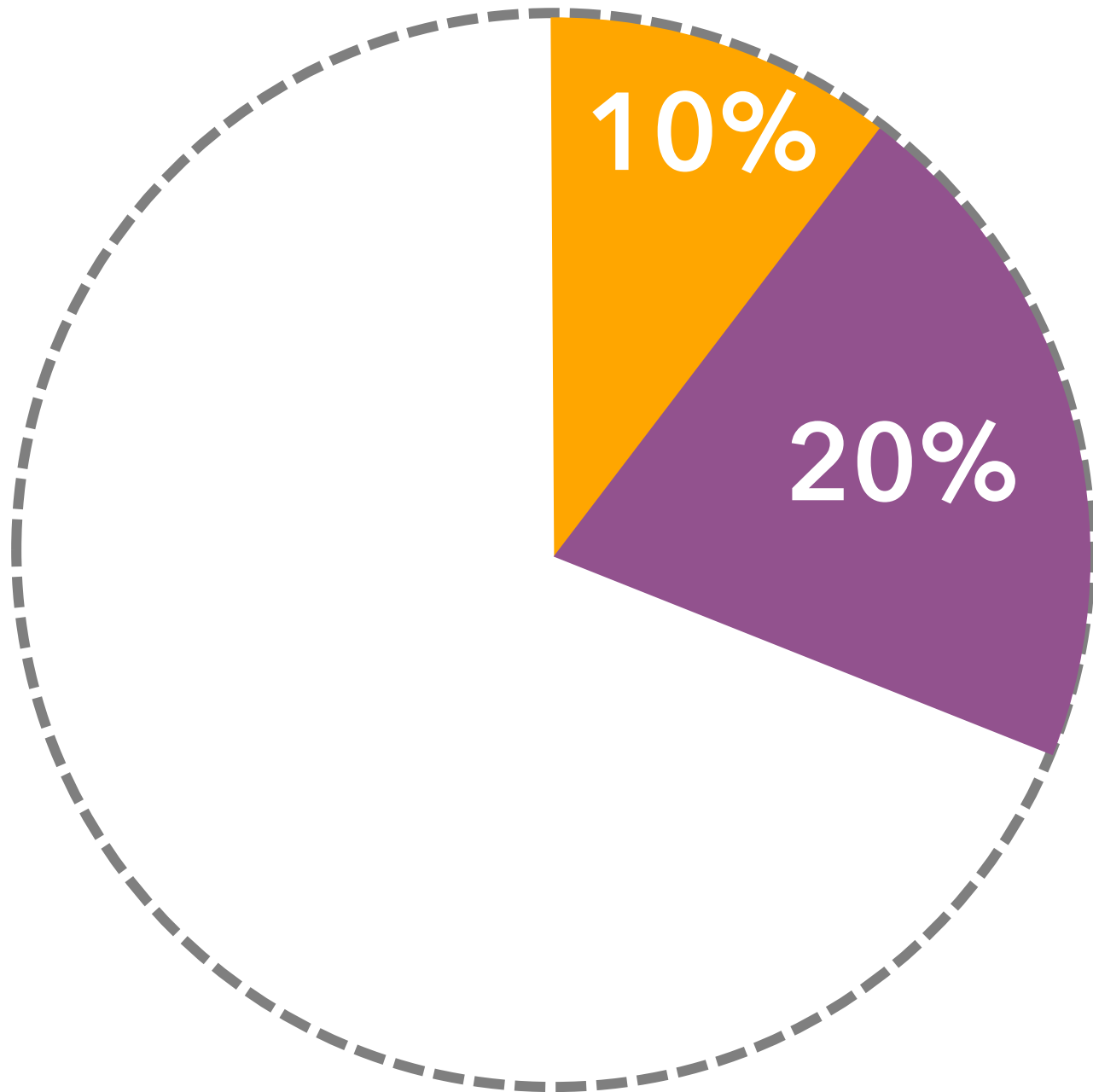


Børn med kræft har  
en overhyppighed af  
evolutionært atypiske  
genforandringer





Børn med kræft har  
en overhyppighed af  
evolutionært atypiske  
Udgørelser



**Kendt  
børnekræftsyndrom**

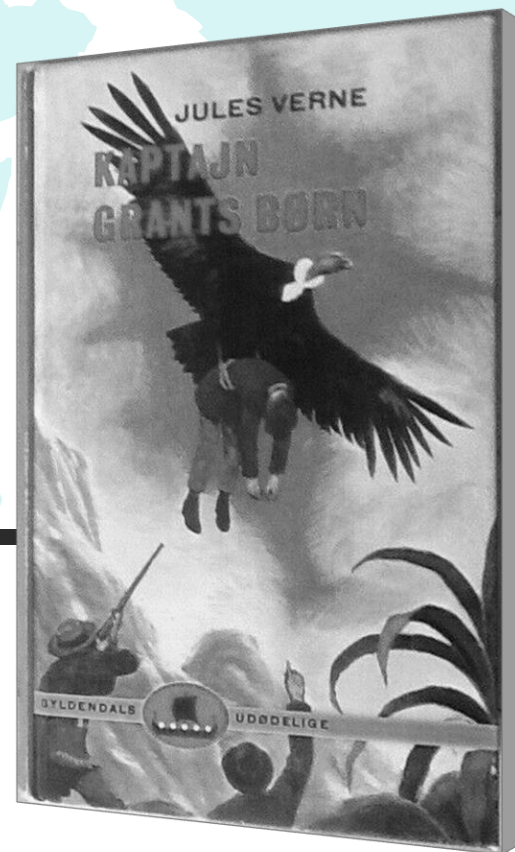
**Endnu ukendt  
børnekræftsyndrom?**

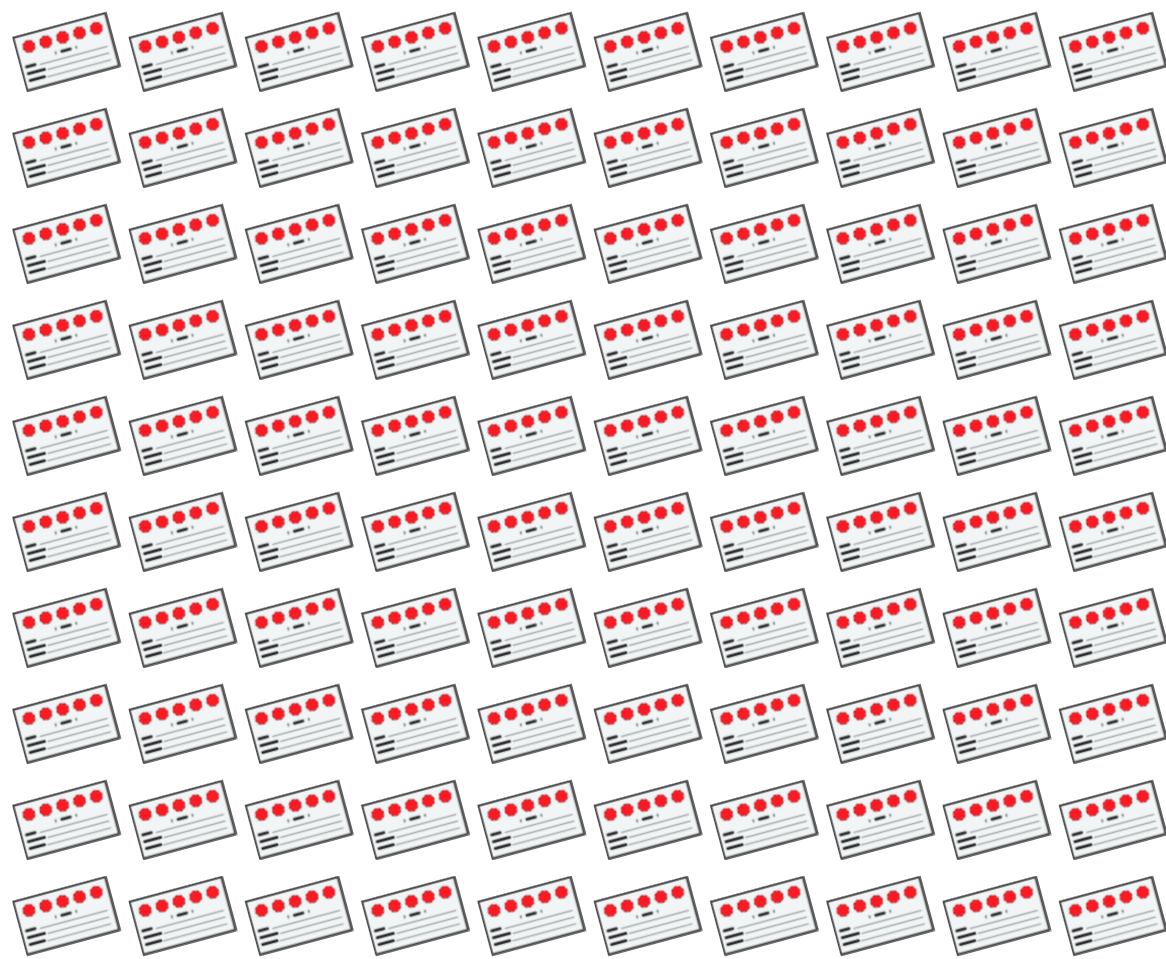


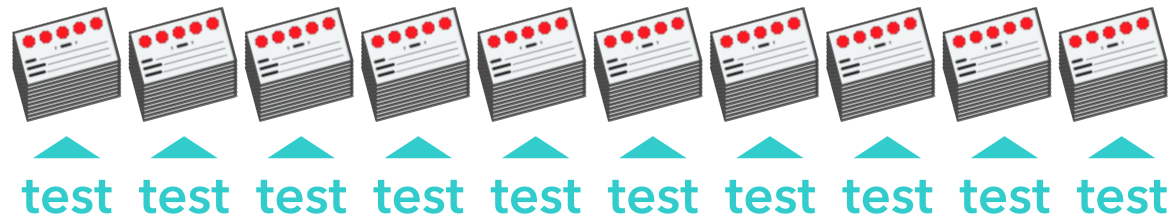
**Bombefly &  
Børnekræft**



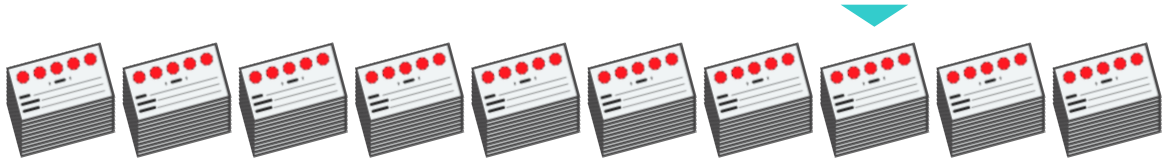
# Kaptajn Grant Problemet

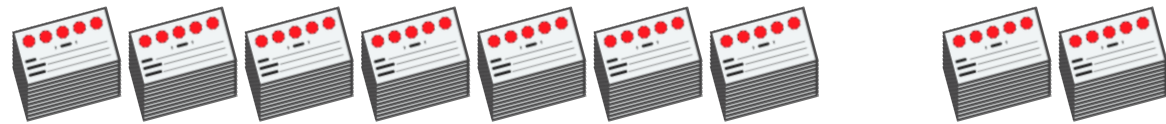






*TP53* mutation



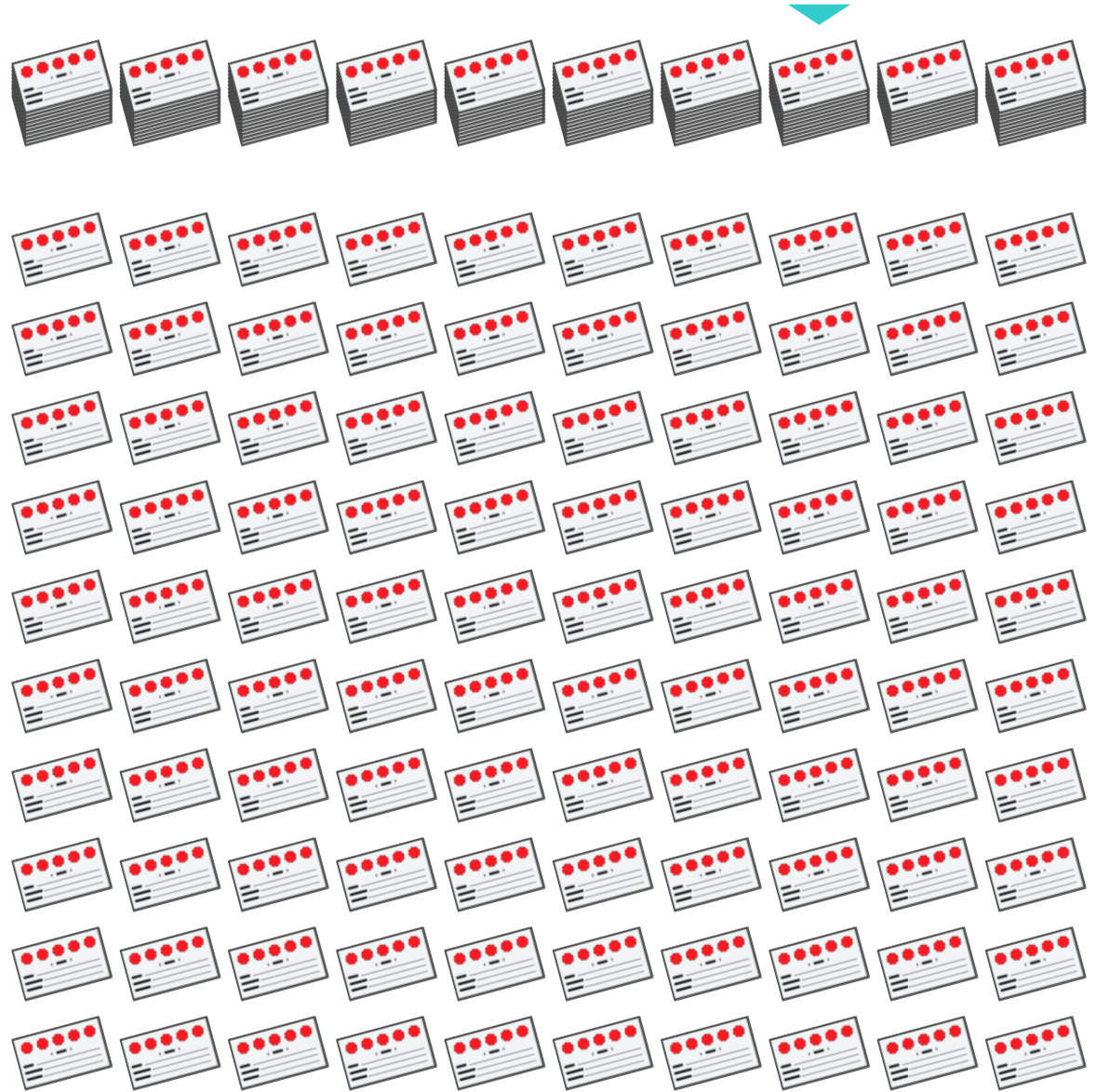


TP53 mutation?

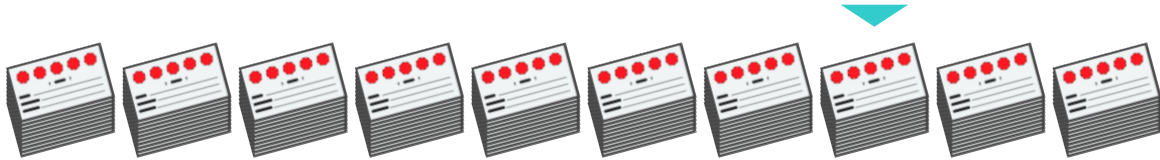




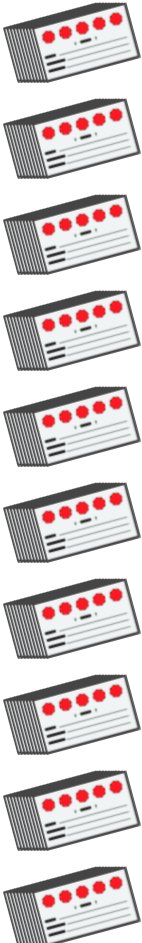
TP53 mutation



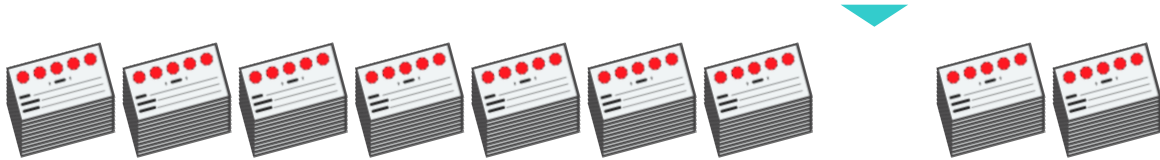
*TP53* mutation



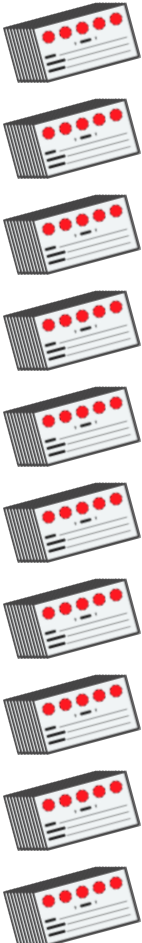
*TP53* mutation



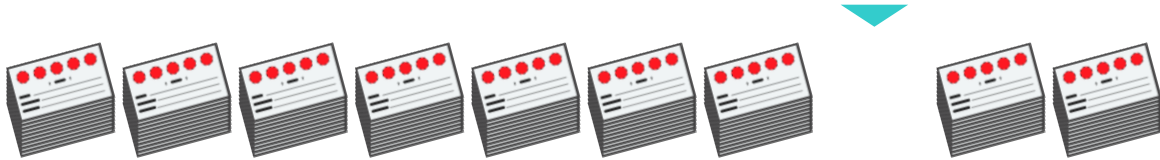
*TP53* mutation



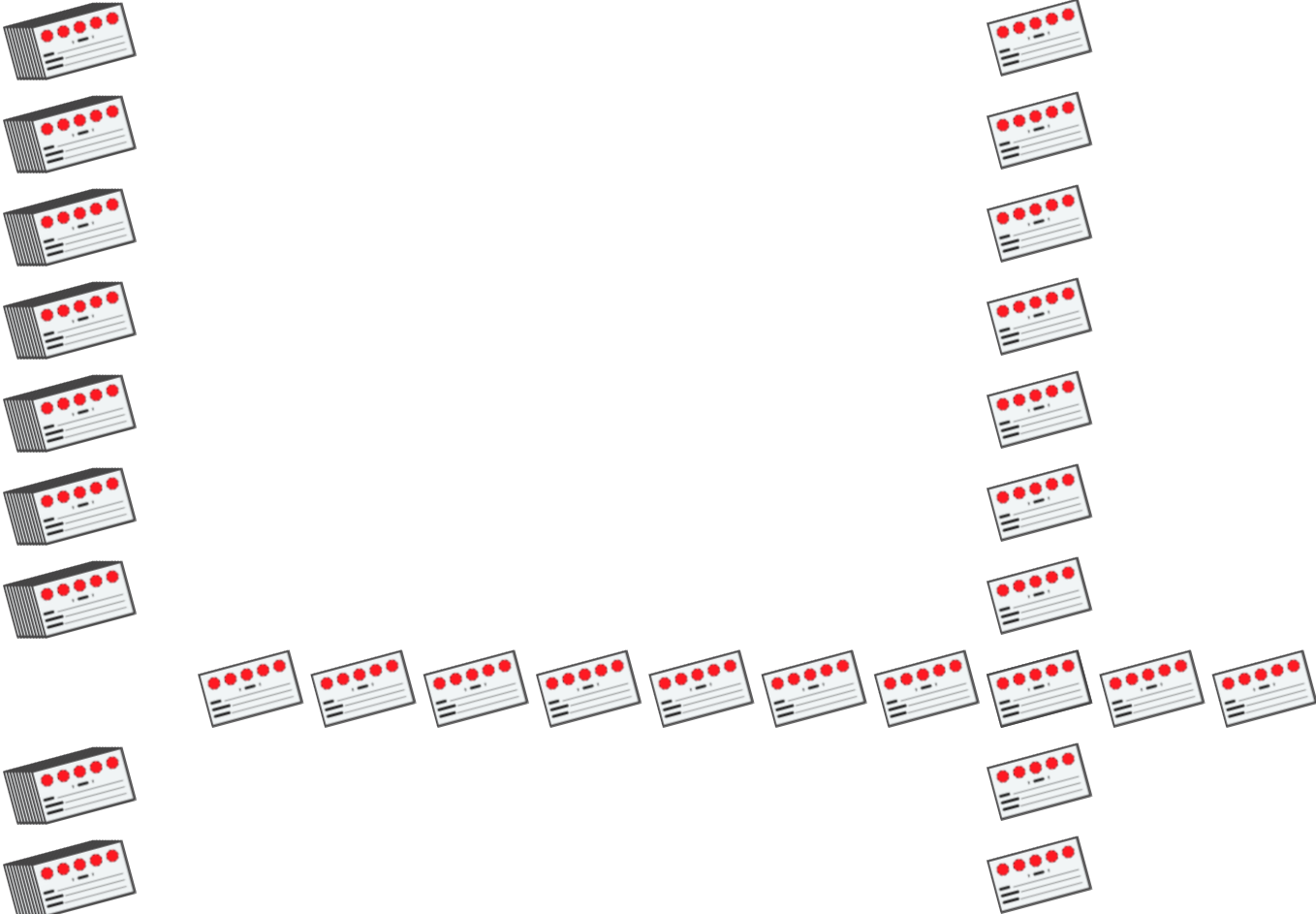
*TP53* mutation

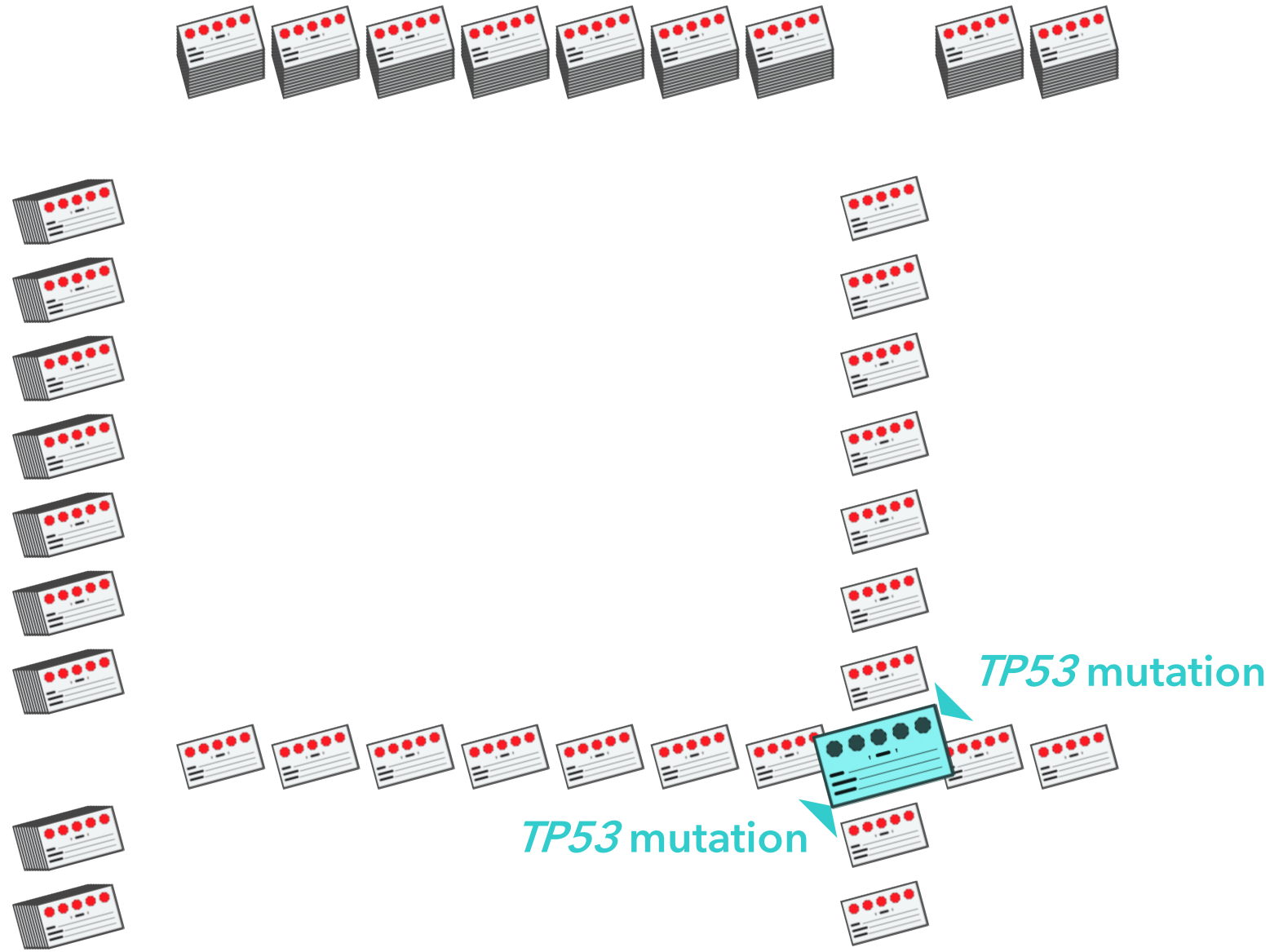


*TP53* mutation



*TP53* mutation





▲▲▲ Diagnose

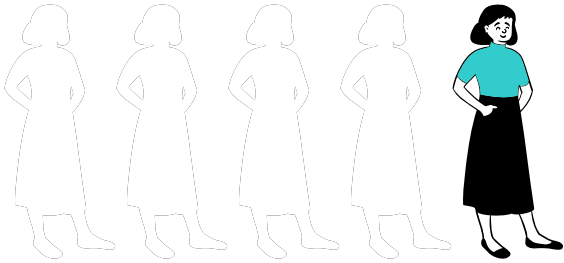
▼▼▼ Omkostninger

**60.000** nyfødte / år

**~15** er som Vega

**↓>50%** børnekræft-dødelighed

*BRCA* mutation



Populationscreening



Sjældne sygdomme





# PREDiSPOSED

Population-based **R**etro- & prospective **E**valuation  
of **D**iagnostic **S**equencing for **P**ediatric & **O**ncogenetic **S**yndromes' **E**arly **D**etection

# STOR TAK TIL...



Kjeld  
Schmiegelow



Karin  
Wadt



Thomas  
v. Overeem Hansen



Simon  
Rasmussen



Henrik  
Hjalgrim



Jonas  
Bybjerg-Grauholm



Christian  
Munch Hagen



Allan  
Lund



Signe Holst  
Søgaard



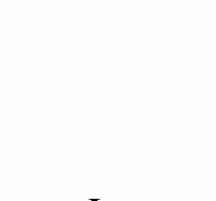
Ayo  
Wahlberg



Jacob Tfelt-  
Hansen



Tania  
Masmas



Lene  
Rottensen

## Peds. cancer screening clinic:

Jesper Brok  
Sabine Grønberg  
Lisa Hjalgrim  
Mimi Kjærsgaard  
Astrid Sehested  
Vera Rasmussen  
Signe Sleiborg  
Helle Schack  
Lillian Hauman

## PREDiSPOSED:

Lene Rottensten  
Signe H. Søgaard  
David Hougaard  
Allan M. Lund  
Marie B.-Hansen  
Tania n. Masmas  
Jacob Tfelt-Hansen

## Bonkolab staff:

Sebina Klica  
Emel Korkmaz

## Genomic medicine:

Maria Rossing  
Lise Ahlborn  
Christina W. Yde  
Frederik O. Bagger  
Filipe G. Vieira

## Broad Inst.:

Konrad Karczewski  
Bram Gorissen  
Hannah Jacobs

## Other collabs:

Astrid Eliassen  
Kim Dalhoff  
MIPOGG group

## Dept. of clinical genetics:

Birgitte Diness  
Mads Bak  
Elsebet Østergaard  
Kirsten Grønsvog  
Zeynep Tümer  
Mathis Hildonen  
Mette Klarskov  
Jack Cowland  
Sophia H.-Hansen

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Henrik Hasle  
Peder Skov Wehner  
Steen Rosthøj

## DTU bioinformatics:

Elena Papaleo  
Adrian Laspiur  
Marianne Helenius  
Kristoffer Rapacki  
Rikke L. Nielsen  
Nikola Tom  
Ramneek Gupta

## PREDiSPOSED Steering:

Merete Lange  
Henrik Ullum  
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Mads Melbye  
Charlotte K. Lautrup  
Jan Johnsen

## STAGING & ICOPE:

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Karin Wadt  
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Thomas Hansen  
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Anna Byrjalsen  
Daniel Dybdal  
Ayo Whalberg  
Anne-Marie Gerdes  
Jane Frederiksen  
Rene Mathiasen  
Anja Hirche  
Solvej Kullegaard  
Astrid Saksager

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Christian Hagen  
Henrik Hjalgrim  
Marie Bækvad-Hansen

## International advisory board:

Michael Walsh  
Christian Kratz  
Nick Hayward

## Bonkolab PhDs, postdocs, nurses, and all staff

## Friends and family!

## THE PATIENTS AND THEIR FAMILIES



## FUNDING

børne | cancer | fonden

Innovation Fund Denmark

