Data-driven childhood cancer precision medicine and research

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Associate Professor, Center for Molecular Medicine, UMC Utrecht

Childhood cancer

Major cause of disease-related death

Childhood cancer survival rate has increased the last decades
to around 75-80% today

Still major cause of disease-related child death in high-income countries

Our mission

princess máxima center
pediatric oncology

To cure every child with cancer, with an optimal quality of life

Our primary use case

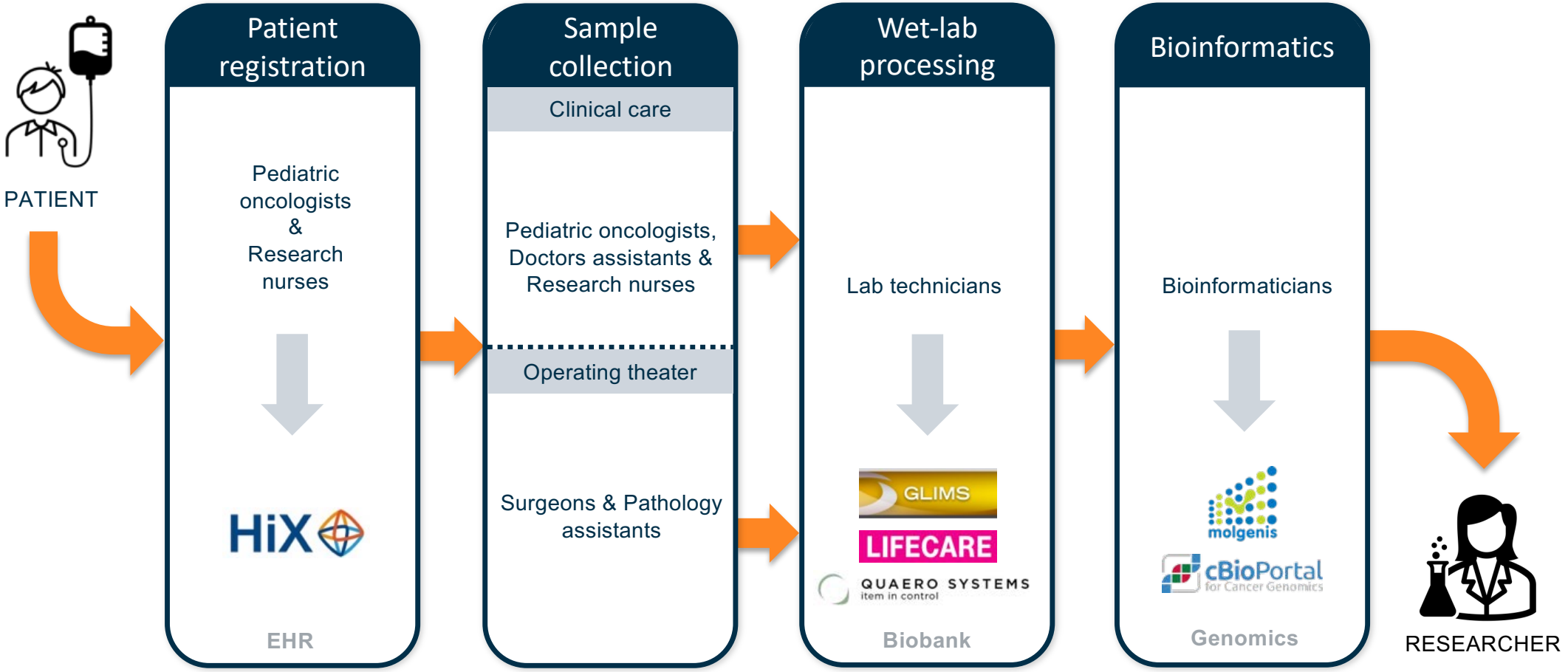
Biobank

Broad informed consent

Data of 2500 patients, sequencing (WGS, RNA-seq) for ~900 patients

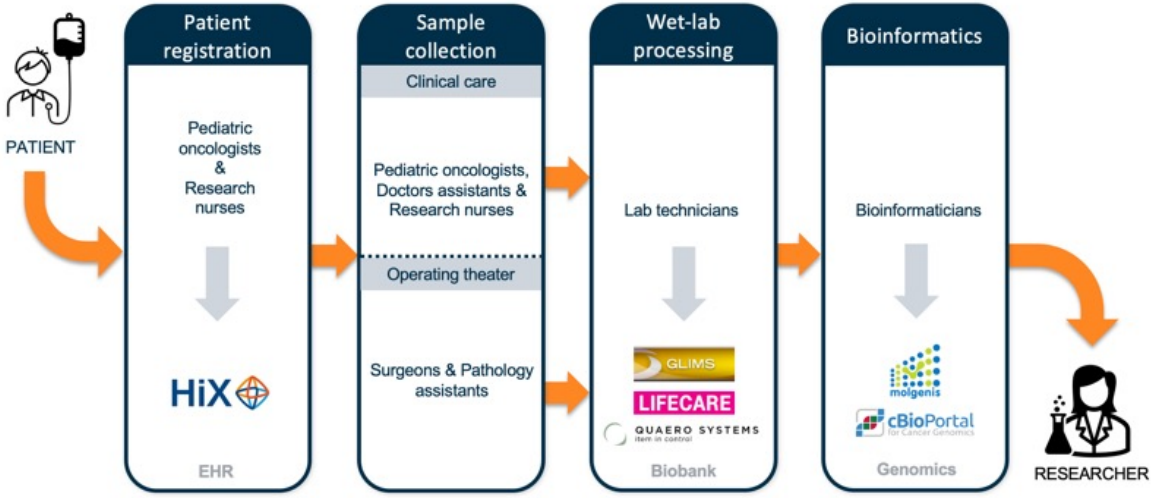
Biobank & Data Access Committee (BDAC)

Biobanking flow



Biobanking flow

Sequencing & bioinformatics

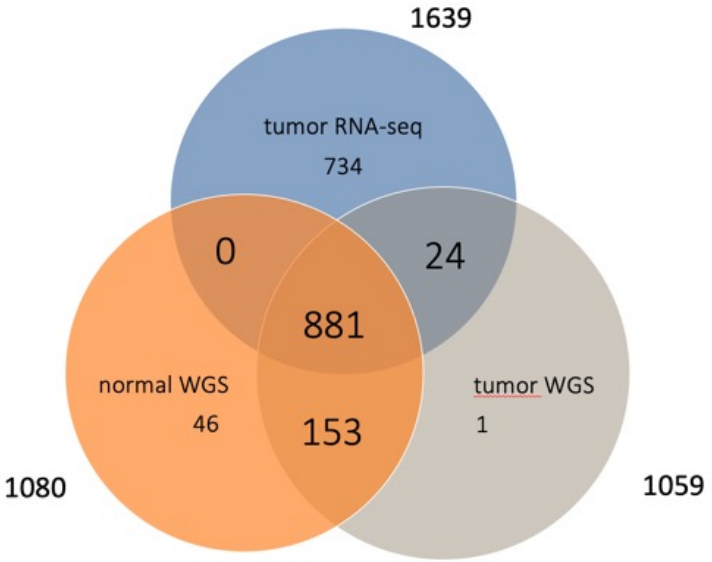


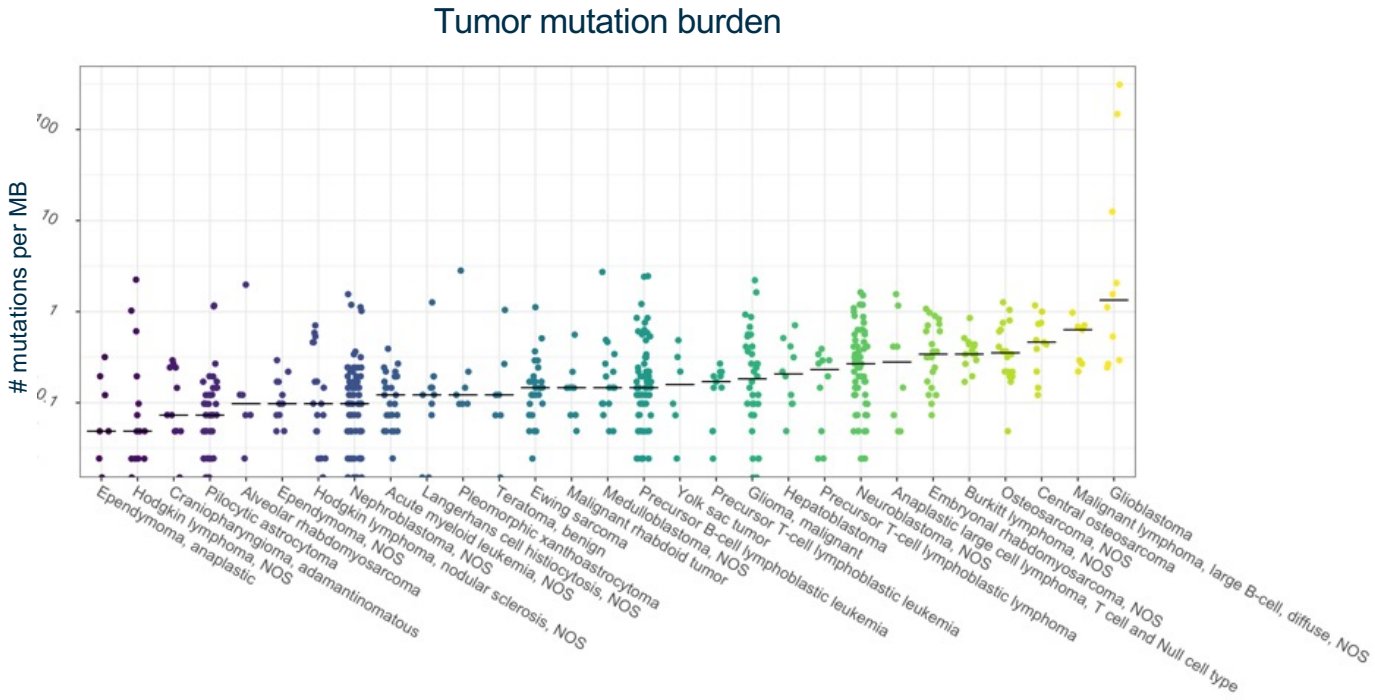
<u>Diagnostics</u>
WES
RNA-seq
DNA methylation

<u>Research</u>
WGS
RNA-seq
DNA methylation

Dutch Childhood Cancer Genome Project

Create a uniform and unique data set of WGS + RNA-seq pediatric cancer genomes for research

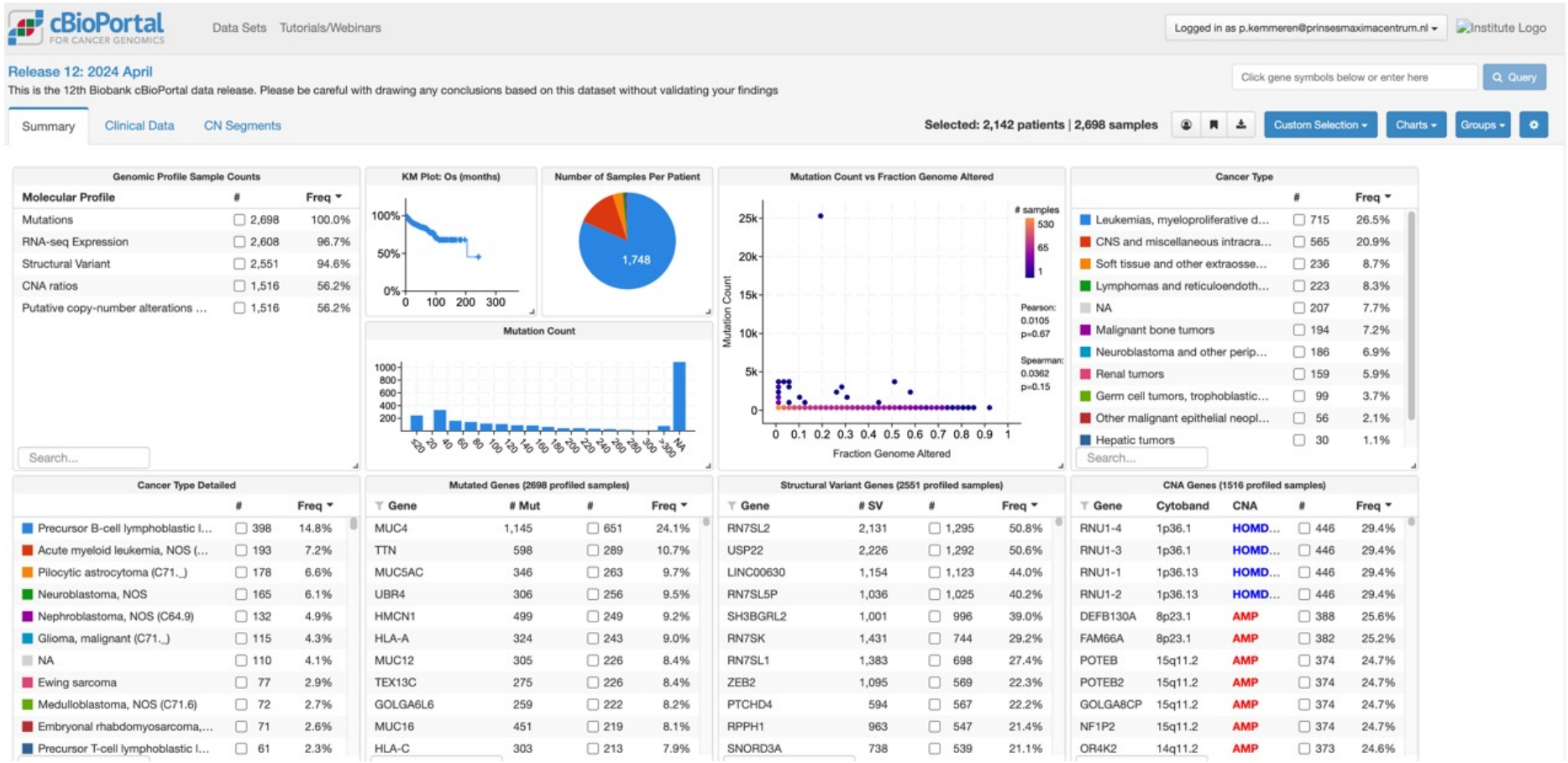




Joanna von Berg, Ianthe van Belzen, Anastasia Spinou, Fleur Wallis, Hinri Kerstens, Jayne Hehir-Kwa

Máxima cBioPortal

Release v12, April 2024, 2,142 patients

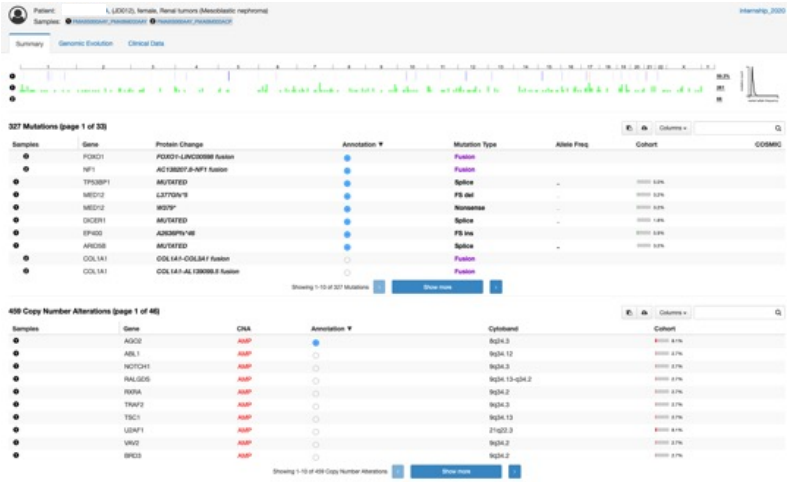


Máxima cBioPortal

Different views on the same data

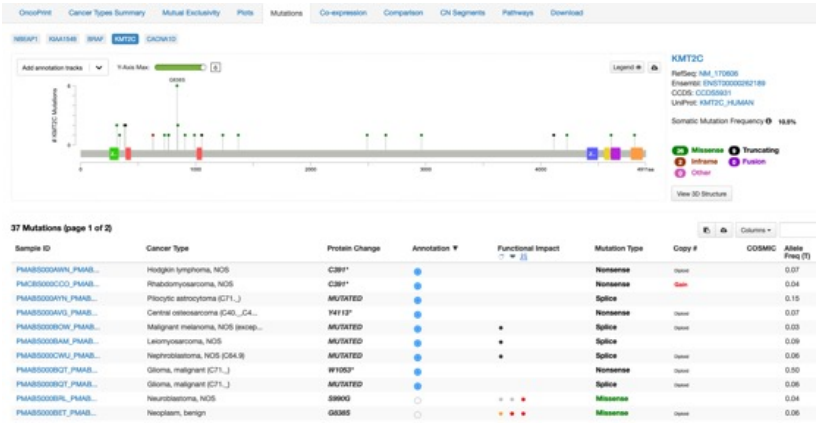
Cohort/study overview

Patient overview

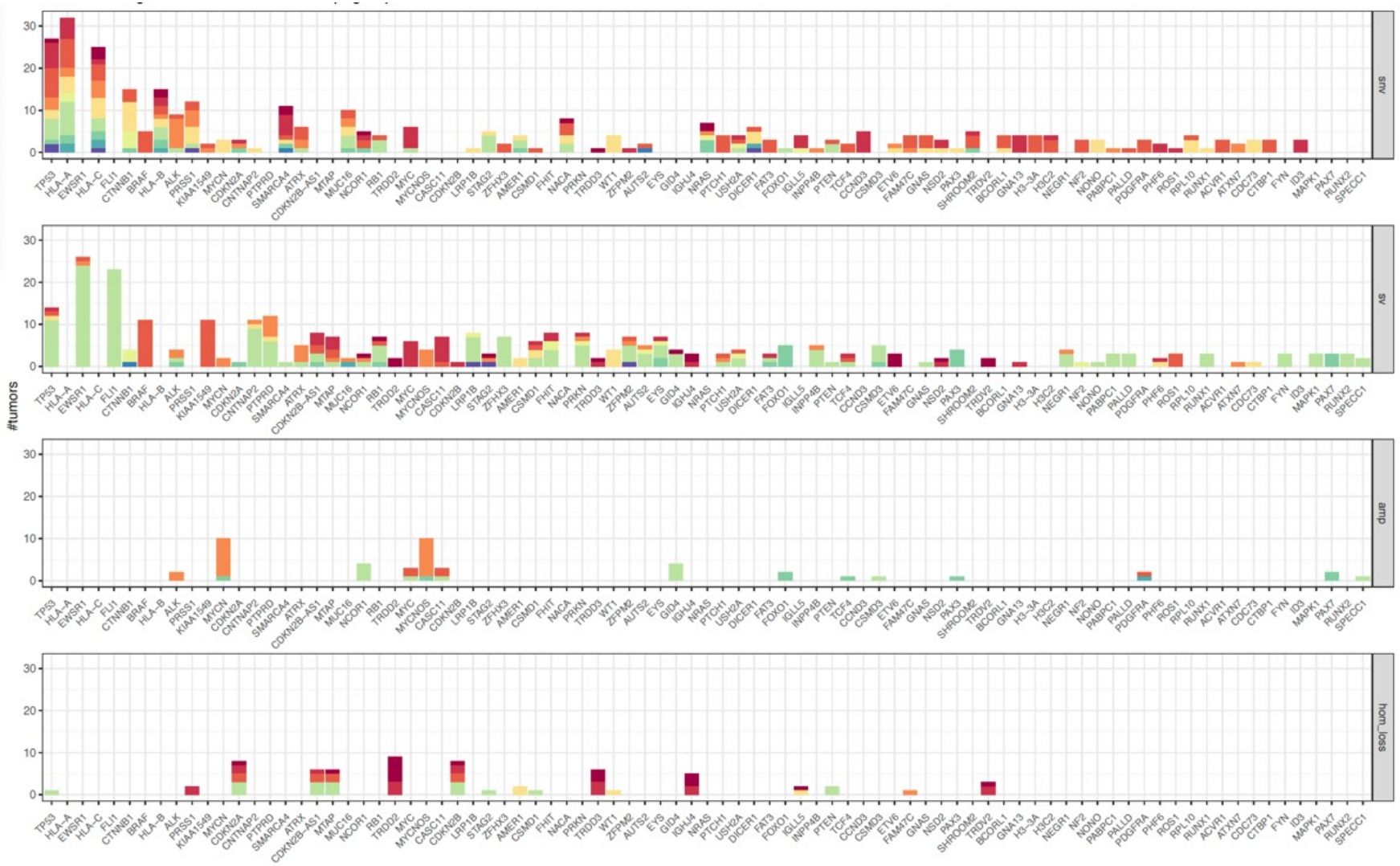


Oncoprint

Gene/mutation level view



Mutational landscape of childhood cancers



From basic tumor biology to clinical utility

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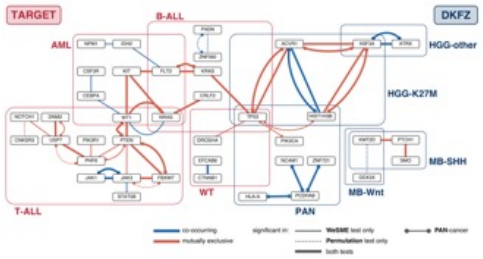
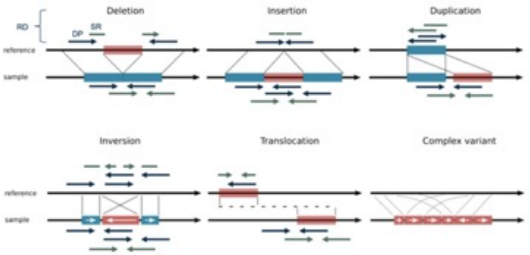
pediatric oncology

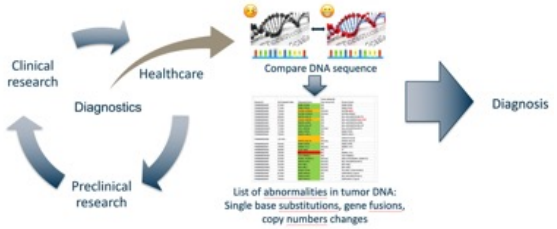
Genetic interactions



Structural variation detection



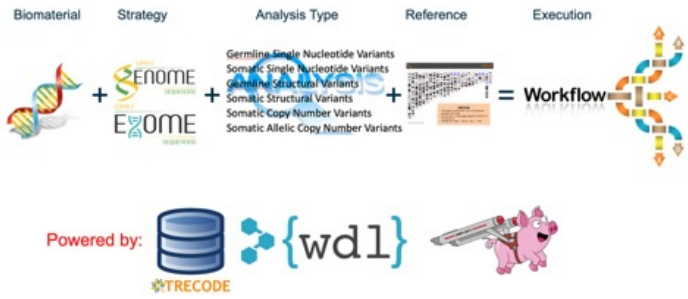
Translational Bioinformatics



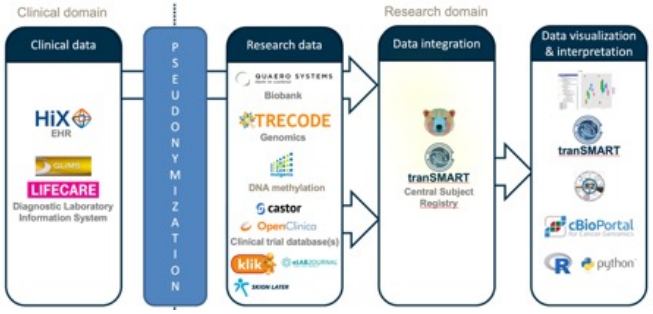
basic research → translational research → Clinical utility

Technology-driven

Biobank Bioinformatics



Data Infrastructure

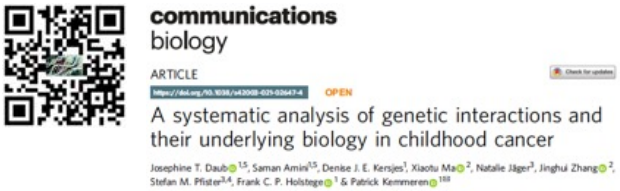


Data Stewardship

From basic tumor biology to clinical utility

princess máxima center
pediatric oncology

Genetic interactions


communications biology

ARTICLE

OPEN

A systematic analysis of genetic interactions and their underlying biology in childhood cancer

Structural variation detection

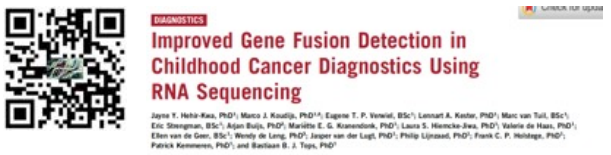

cancers

MDPI

Article

Molecular Characterization Reveals Subclasses of 1q Gain in Intermediate Risk Wilms Tumors

Translational Bioinformatics

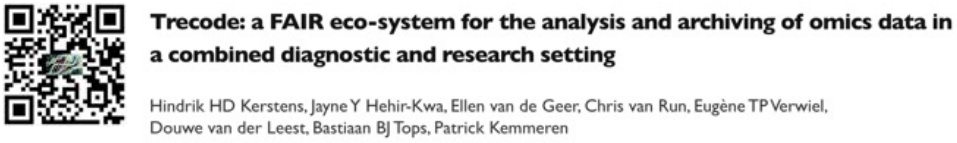

DIAGNOSTICS

Improved Gene Fusion Detection in Childhood Cancer Diagnostics Using RNA Sequencing

basic research → translational research → Clinical utility

Technology-driven

Biobank Bioinformatics


Trecode: a FAIR eco-system for the analysis and archiving of omics data in a combined diagnostic and research setting

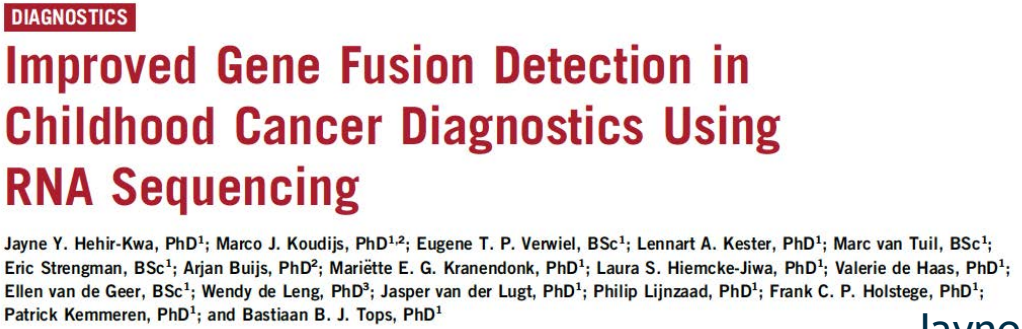
Hindrik HD Kerstens, Jayne Y Hehir-Kwa, Ellen van de Geer, Chris van Run, Eugène TP Verwiel, Douwe van der Leest, Bastiaan BJ Tops, Patrick Kemmeren

Data Infrastructure

Data Stewardship

RNA-seq gene fusion detection for precision oncology & precision medicine

Hehir-Kwa, Koudijs et al, JCO Prec Onc 2022



DIAGNOSTICS

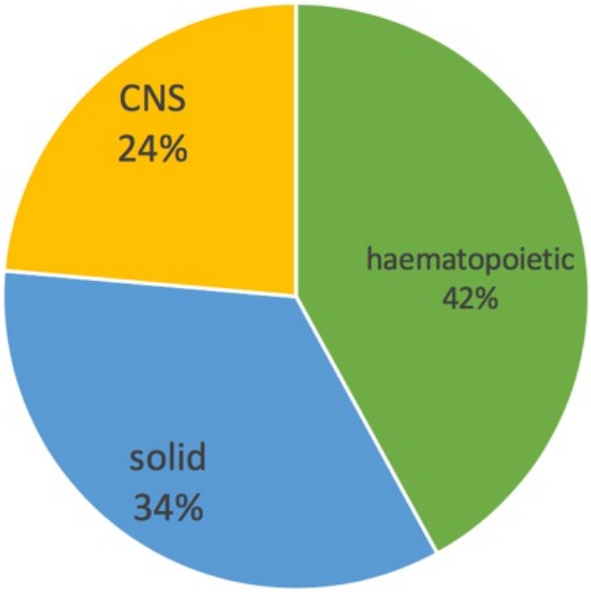
Improved Gene Fusion Detection in Childhood Cancer Diagnostics Using RNA Sequencing

Jayne Y. Hehir-Kwa, PhD[1]; Marco J. Koudijs, PhD[1,2]; Eugene T. P. Verwiel, BSc[1]; Lennart A. Kester, PhD[1]; Marc van Tuil, BSc[1]; Eric Strengman, BSc[1]; Arjan Buijs, PhD[2]; Mariëtte E. G. Kranendonk, PhD[1]; Laura S. Hiemcke-Jiwa, PhD[1]; Valerie de Haas, PhD[1]; Ellen van de Geer, BSc[1]; Wendy de Leng, PhD[3]; Jasper van der Lugt, PhD[1]; Philip Lijnzaad, PhD[1]; Frank C. P. Holstege, PhD[1]; Patrick Kemmeren, PhD[1]; and Bastiaan B. J. Tops, PhD[1]

Jayne Hehir-Kwa, Marco Koudijs, Bas Tops

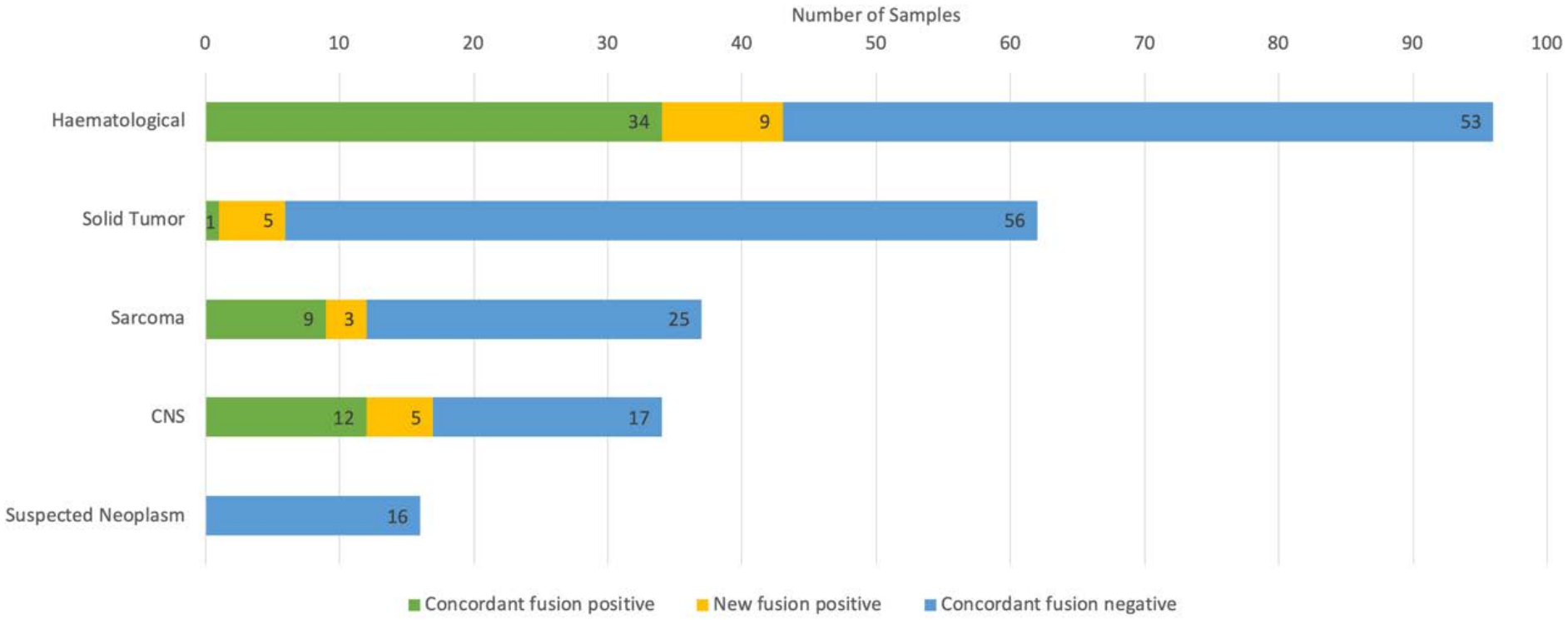
RNA-seq gene fusion detection in diagnostics

257 consecutive patients from 1st December 2018 until 31 May 2019



RNA-seq gene fusion detection in diagnostics

Increased sensitivity of clinically relevant events



No events missed

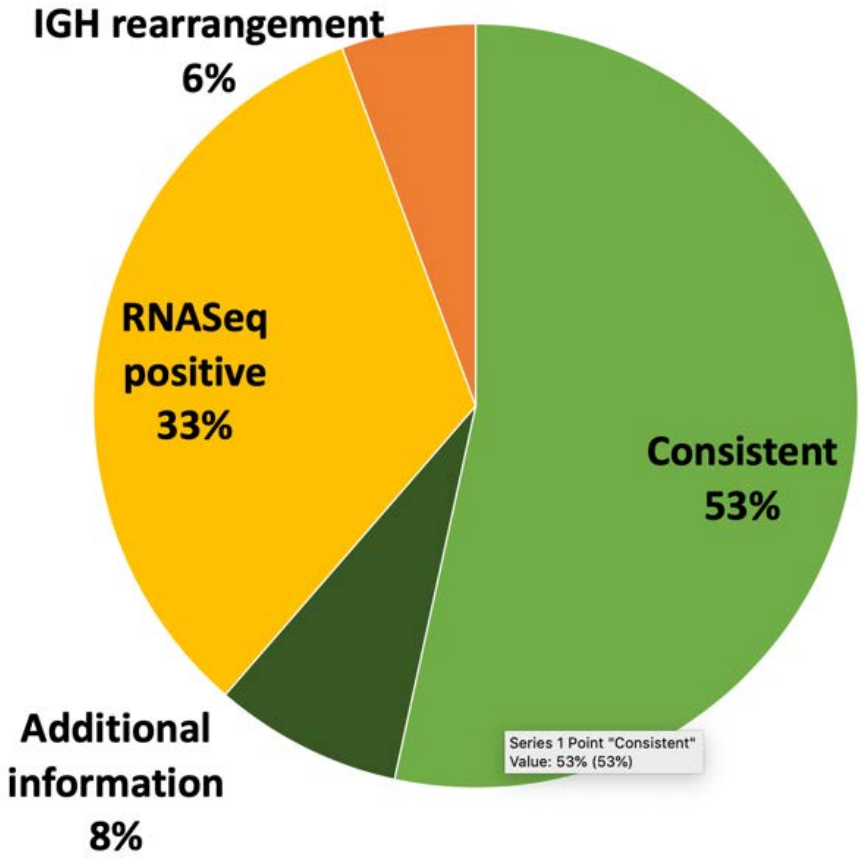
>40% increase in clinically relevant events (22%-> 36%)

RNA-seq gene fusion detection in diagnostics

The fusion positive cases

Additional information
- Fusion partner
- More accurate breakpoint

Additional events
- Not tested
- Atypical breakpoints
- IGH rearrangements

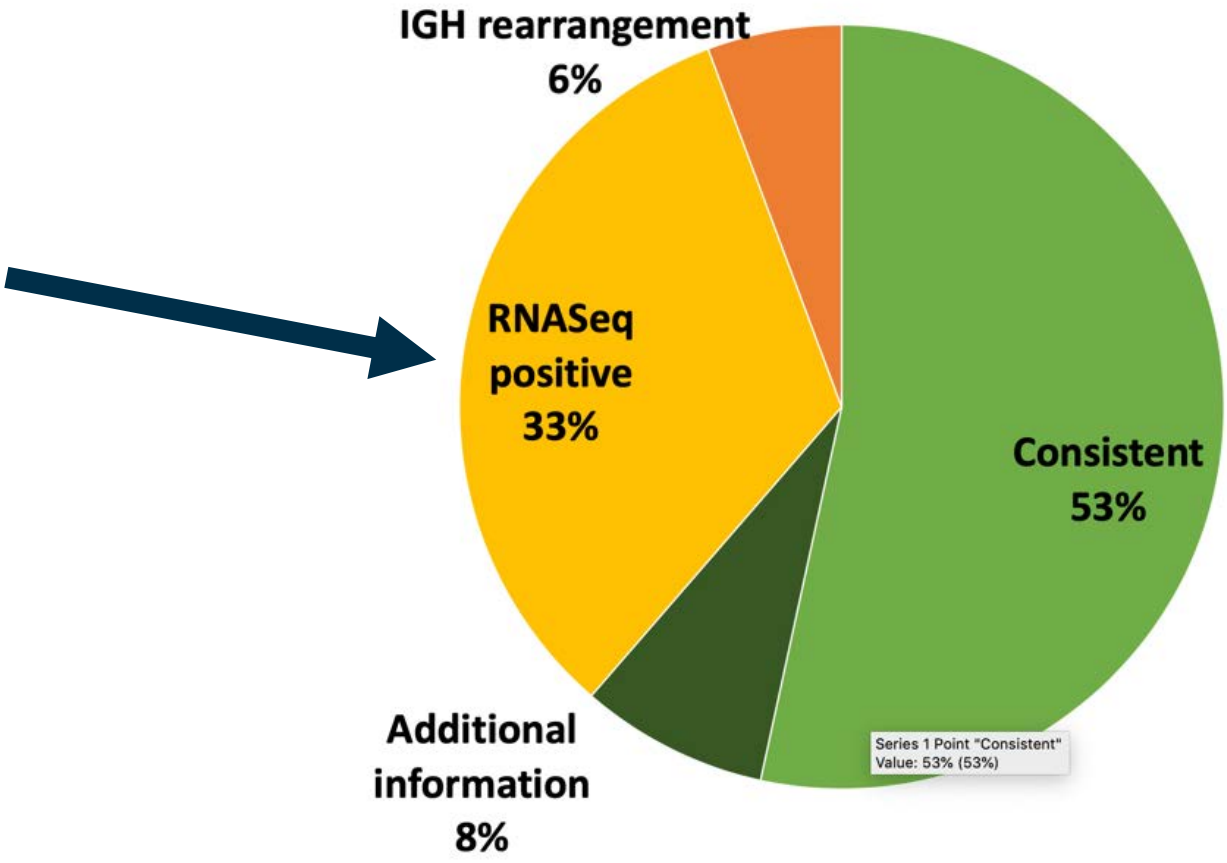


RNA-seq gene fusion detection in diagnostics

The fusion positive cases

4 new druggable gene fusions

- ZCCHC8-ROS1
- PPP1CB-ALK
- EML4-ALK
- EML4-NTRK3



Acknowledgements

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Eugène Verwiel
Hinri Kerstens
Alex Janse
John Baker-Hernandez
Sam de Vos
Jet Zoon
Marcel Santoso
Victoria Cruz
Sotiris Niarchos

Richard Gremmen
Shashi Badloe
Kim Verhagen
Josephine Daub
Denise Kersjes
Saman Amini

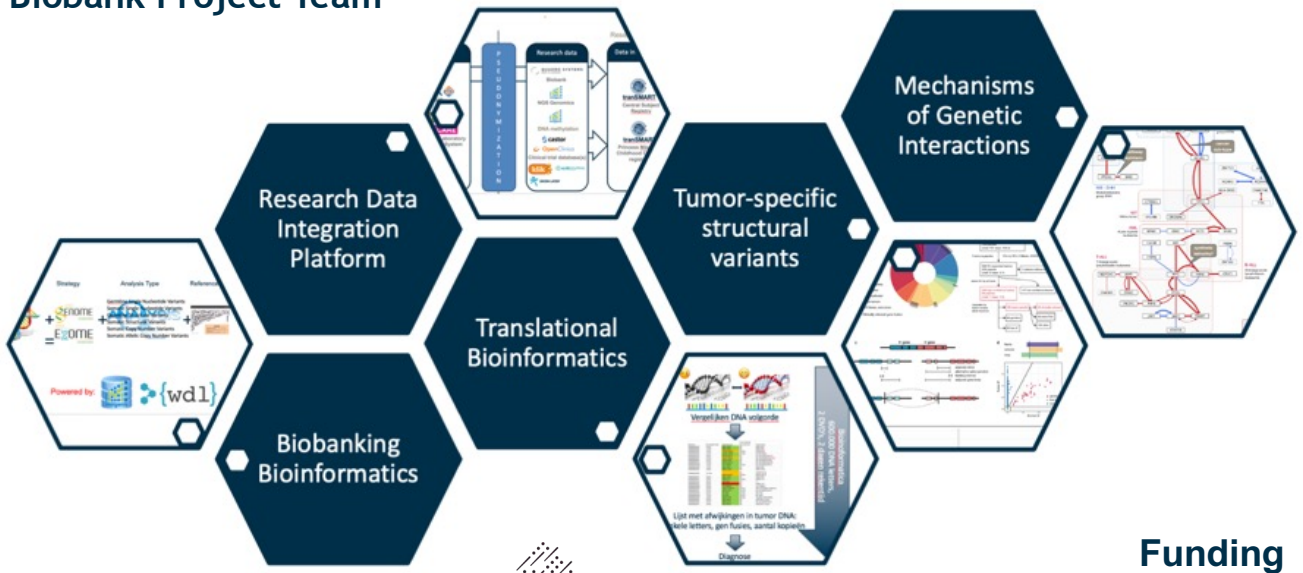
Diagnostic lab

Bas Tops
Marco Koudijs
Marc van Tuijl
Lennart Kester

Trial & Data Centrum

IDT

Biobank Project Team



Funding