

Access, query and view your translational research study in **cBioPortal**: *the MEDOCC use case*

Remond J.A. Fijneman

Translational Gastrointestinal Oncology

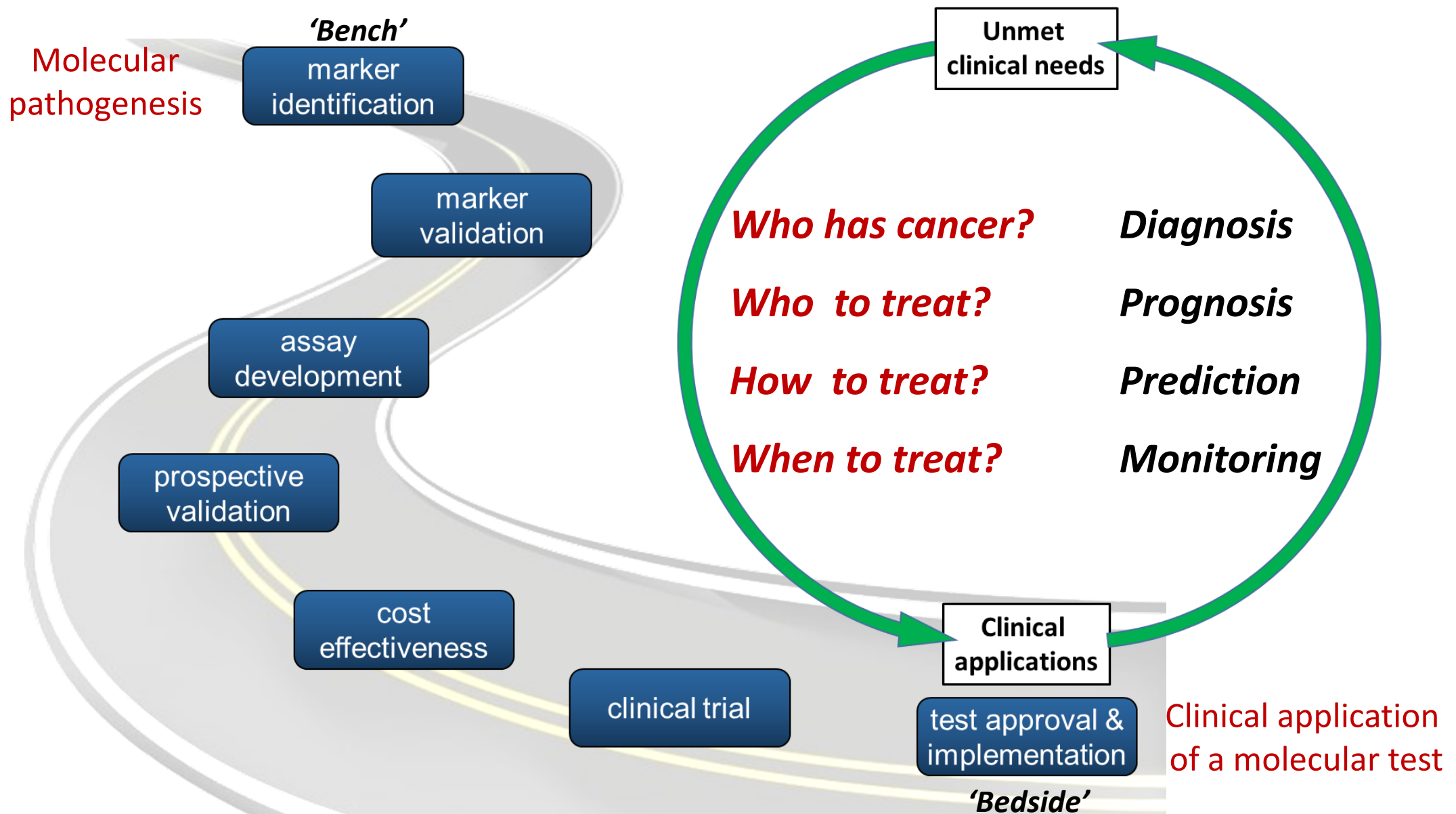


*X-omics workshop #2
Multi-omics integration tools and platforms
10 Feb 2021*

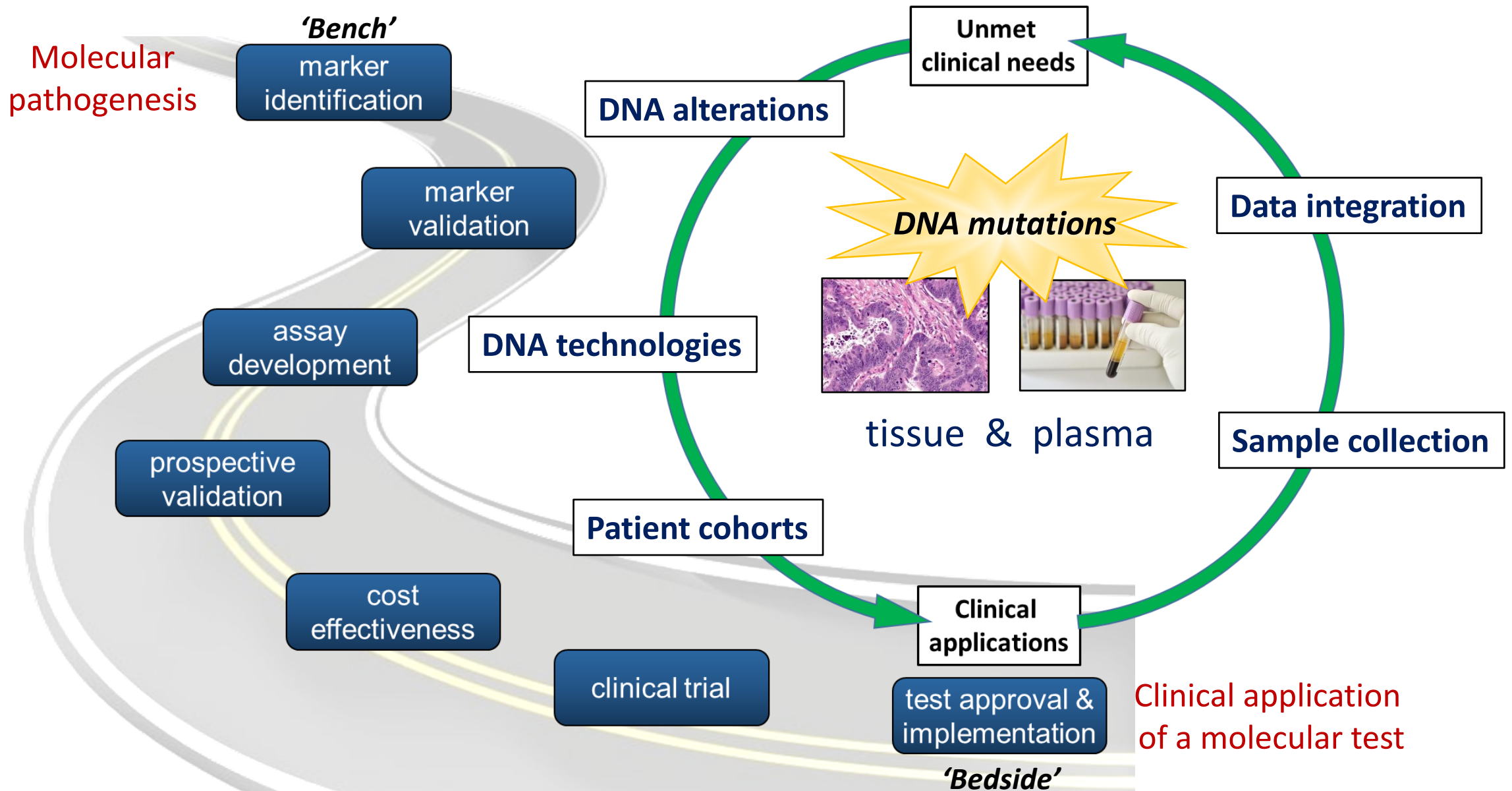
Overview

- Position of cBioPortal in the translational research landscape
- PLCRC-MEDOCC use case
- Future perspectives

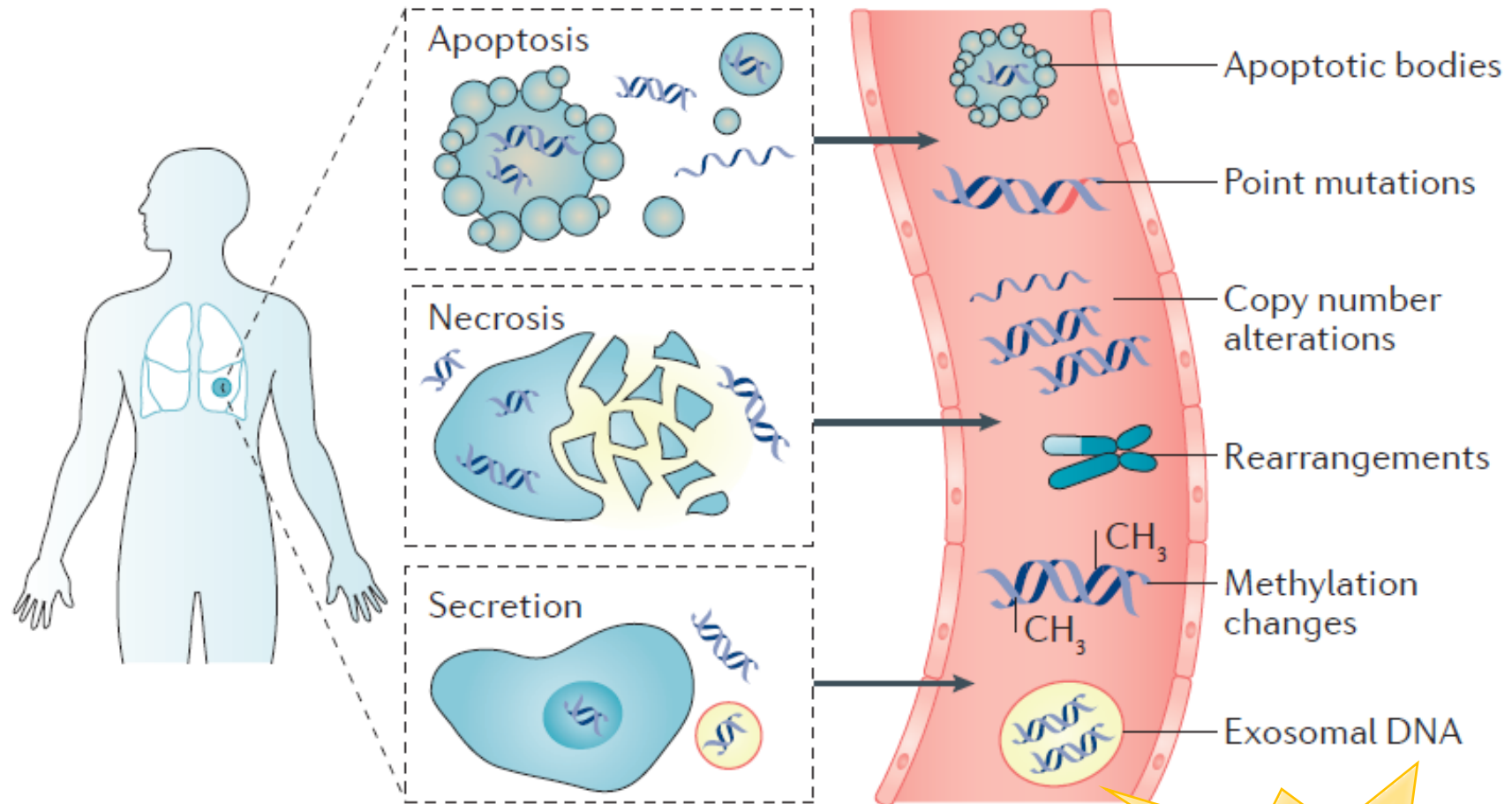
Translational Research - biomarkers



Translational Research - biomarkers



Cell-free circulating tumor DNA (ctDNA)



Wan et al., Nat Rev Cancer 17:223-238 (2017)

DNA mutations

Multidisciplinary team

clinical trials & medical oncology

clinical
chemistry

ctDNA
technology

molecular
biology

pathology
research IT

HTA
modeling



Miriam
Koopman



Geraldine
Vink



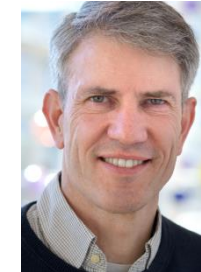
Kees
Punt



Daan van
den Broek



Victor
Velculescu



Remond
Fijneman



Gerrit
Meijer

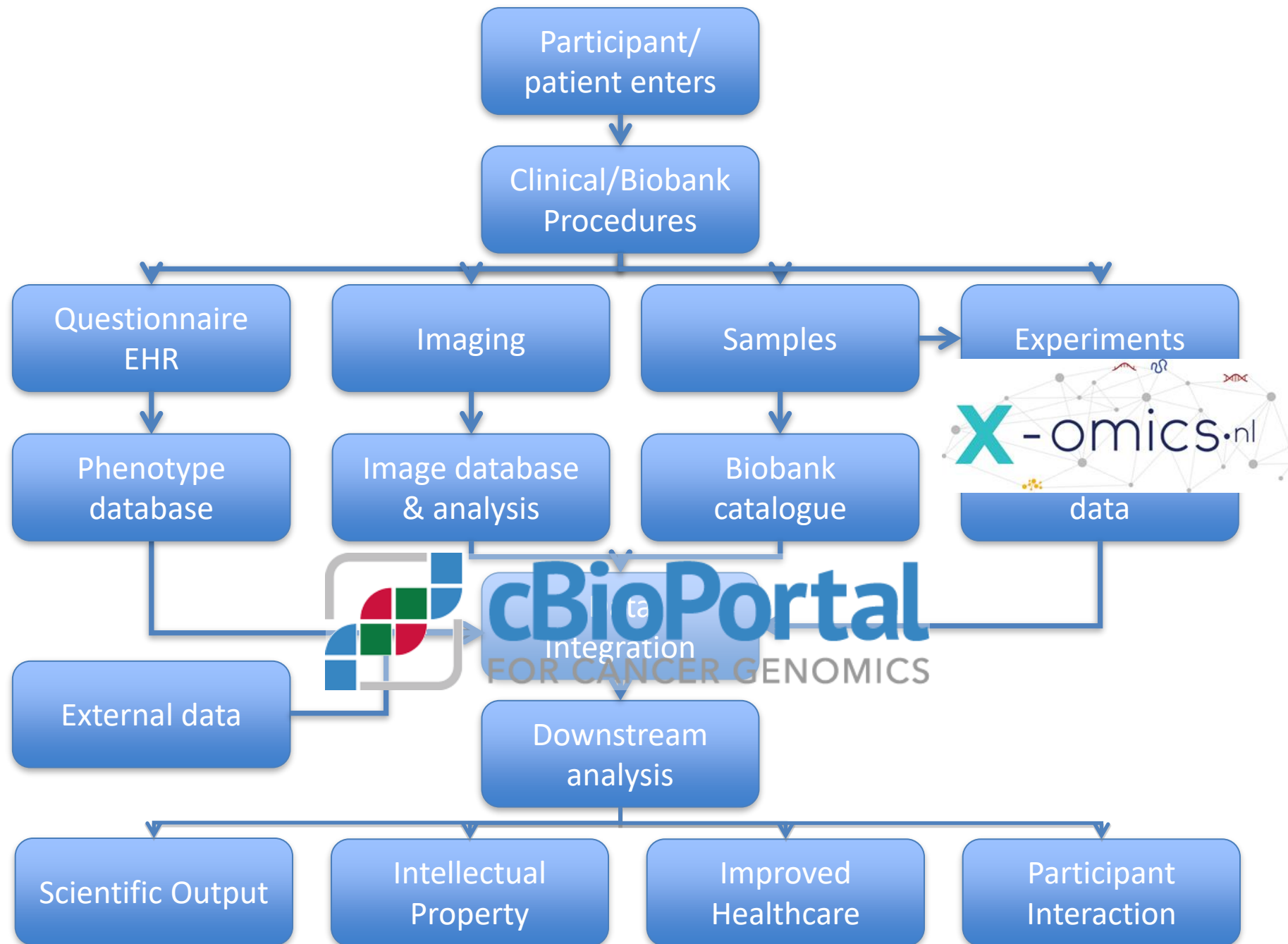


Veerle
Coupé



Multicenter ctDNA studies

Clinical need	CRC stage	Cohort	Patient #	Clinical question
prognosis	II	MEDOCC (PLCRC)	850	Who to offer chemotherapy
prognosis	III	PROVENC3 (PLCRC)	267	Who <i>not</i> to offer chemotherapy
prediction, monitoring	IV Not liver limited	ORCA (PLCRC)	100	Primary/acquired anti-EGFR resistance Monitoring treatment response
prediction, monitoring	IV Liver limited	CAIRO5	564	Primary/acquired anti-EGFR resistance Monitoring treatment response
monitoring	IV Peritoneum	CAIRO6	350	Monitoring treatment response



cBioPortal

- The cBioPortal is an open-access resource for interactive exploration of multidimensional cancer genomics data sets.
- The cBioPortal significantly lowers the barriers between complex genomic data and cancer researchers* who want rapid, intuitive, and high-quality access to molecular profiles and clinical attributes from large-scale cancer genomics projects. [**read: non-bioinformaticians*]
- Started with TCGA data, has been growing ever since




Cerami et al. *Cancer Discovery* 2012.




Gao et al. *Science Signaling* 2013.









Please cite: Cerami et al., 2012 & Gao et al., 2013




Search...




42 samples   

110 samples   

64 samples   

38 samples   

75 samples   

16 samples   

 Explore Selected Studies

"This portal is truly the greatest thing since sliced bread. I am making discoveries with it not only in

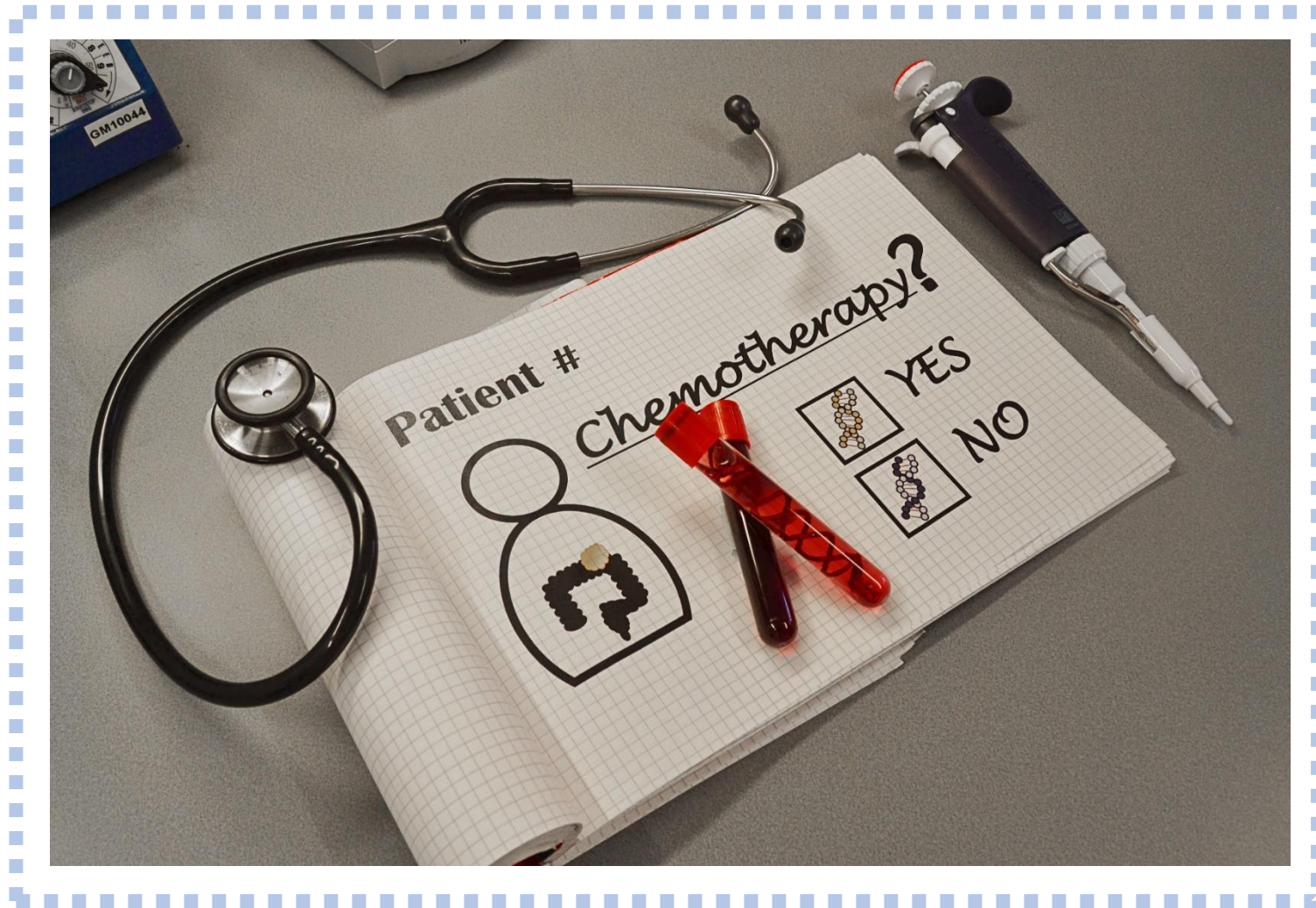
cBioPortal

- The cBioPortal for Cancer Genomics was originally developed at Memorial Sloan Kettering Cancer Center (MSK)
 - a.o. by JJ Gao, Niki Schultz
- The public cBioPortal site is hosted by the Center for Molecular Oncology at MSK.
- The cBioPortal software is now available under an open source license via GitHub.
- The software is now developed and maintained by a multi-institutional team, consisting of MSK, the Dana Farber Cancer Institute, Princess Margaret Cancer Centre in Toronto, Children's Hospital of Philadelphia, The Hyve in the Netherlands, and Bilkent University in Ankara, Turkey.

Overview

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To treat or not to treat, that is the question...



Prospective Dutch CRC cohort (PLCRC)

Stage I, II, III, IV colorectal cancer

Observational:



Clinical data



Tissue



Blood



PROMs

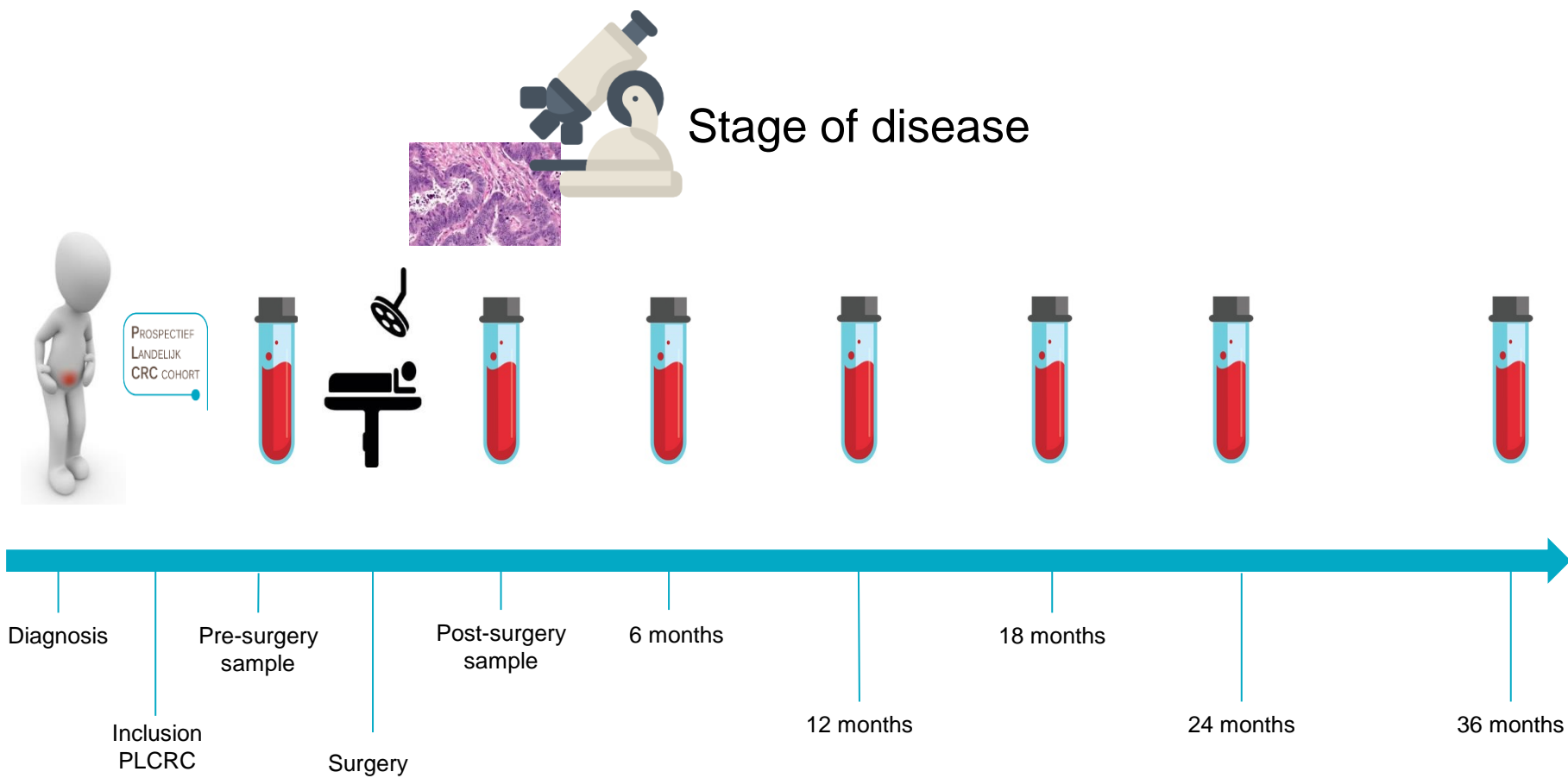


Interventional:

Trials within Cohorts
(TwiCs)

MEDOCC

PLCRC-MEDOCC





PLCRC-MEDOCC



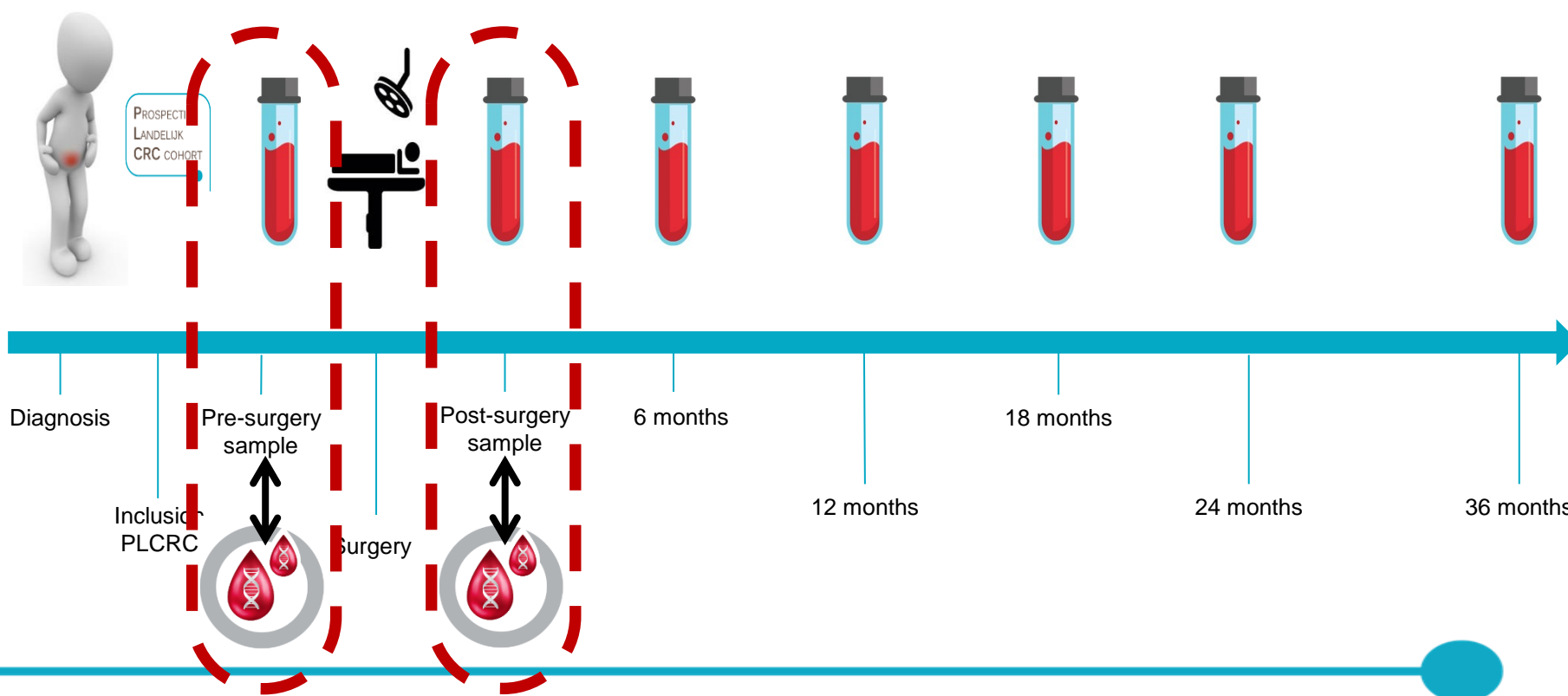
Dave van
der Kruijssen



Carmen
Rubio Alarcón

Stage II MEDOCC: *Molecular Early Detection of Colorectal Cancer*

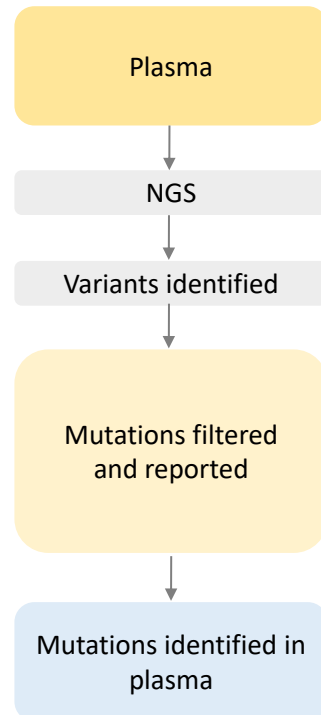
Stage III PROVEN3: *PROgnostic Value of Early Notification by Ctdna in Colon Cancer stage 3*



ctDNA mutation analysis for MRD detection



Jill Phallen



Targeted error correction sequencing

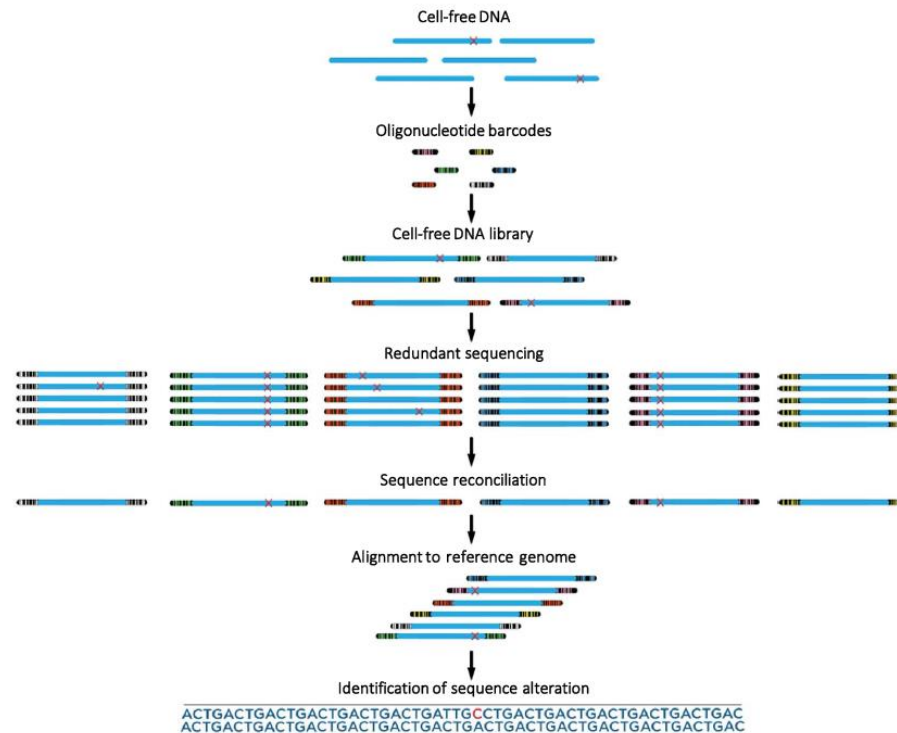
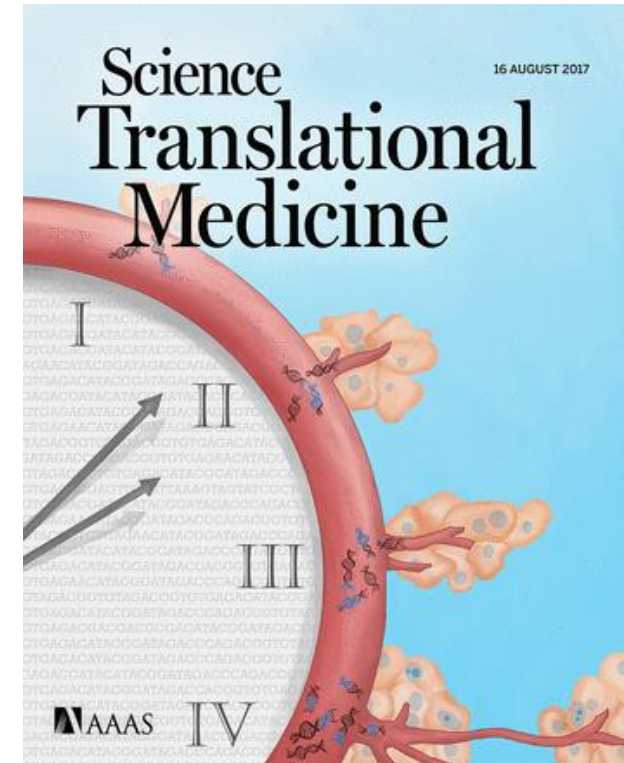


Fig. 1. Schematic of the TEC-Seq method. cfDNA is extracted from the blood and converted to a genomic library through ligation of a pool containing a small number of dual-indexed code adapters. The resulting cfDNA library is captured and redundantly sequenced to produce multiple duplicates of each DNA fragment. Sequence reconciliation among duplicate fragments identifies the original DNA molecules with the same start and end position and exon. **KRAS, BRAF, APC, TP53, 54 more**

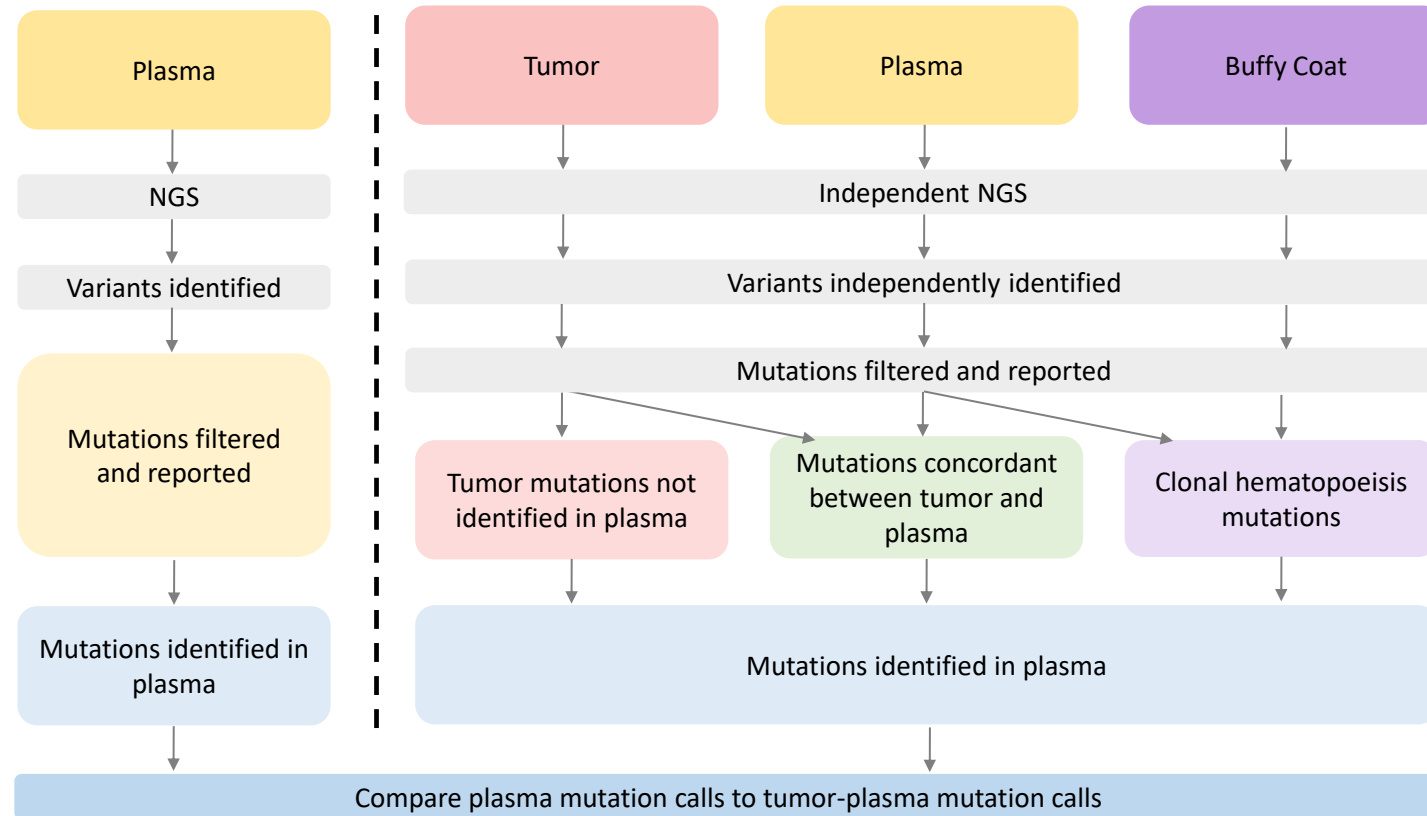


Phallen et al., *Sci Transl Med* 9 (2017)

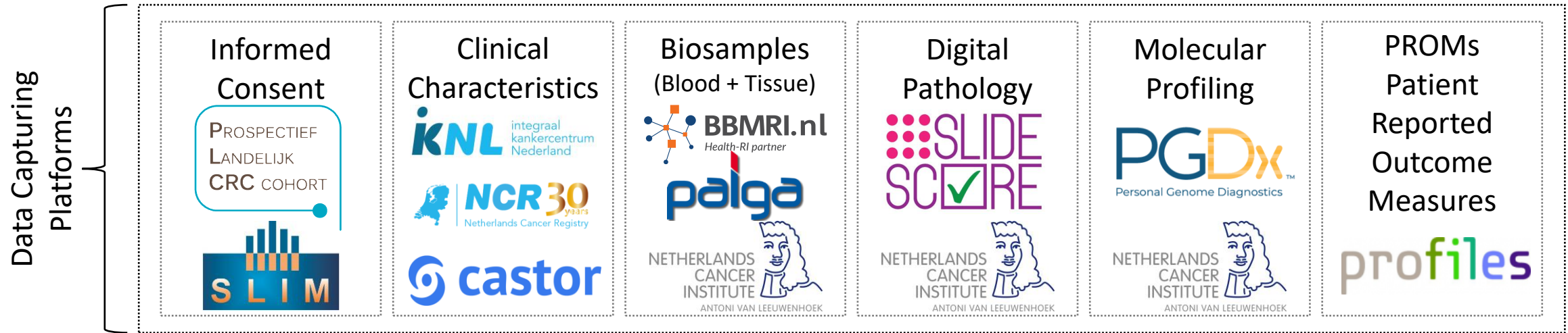
ctDNA mutation analysis for MRD detection



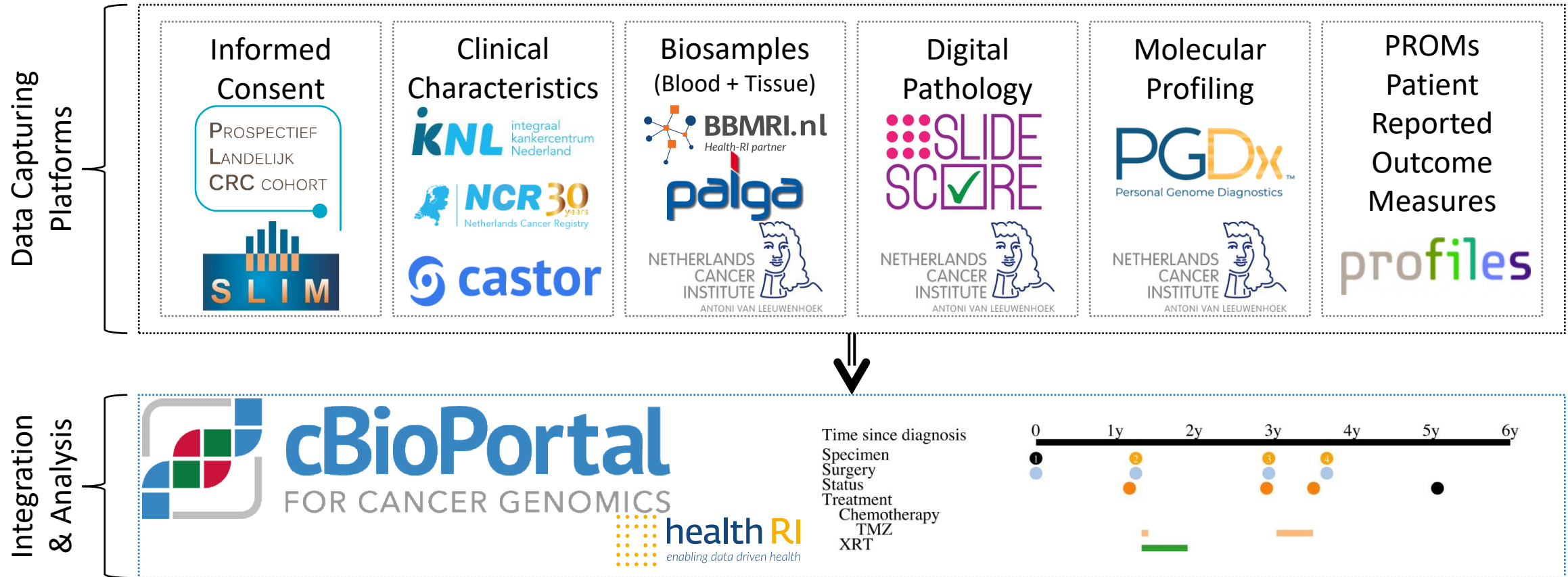
Jill Phallen



Capture data for translational research



Capture data for translational research





<https://www.health-ri.nl>

National initiative to facilitate an integrated health data infrastructure accessible to researchers, citizens and care providers.



70+ organizations



European infrastructure
for translational medicine



← [Services](#)

cBioPortal

Explore, visualize, analyze, and share multidimensional genomics data sets



[About](#) [Getting Started](#) [Support](#) [Further information](#)

About

The Health-RI cBioPortal provides a web-based resource for researchers to explore, visualize, analyze, and share multidimensional cancer genomics data sets as well as other studies with multidimensional genomics data.



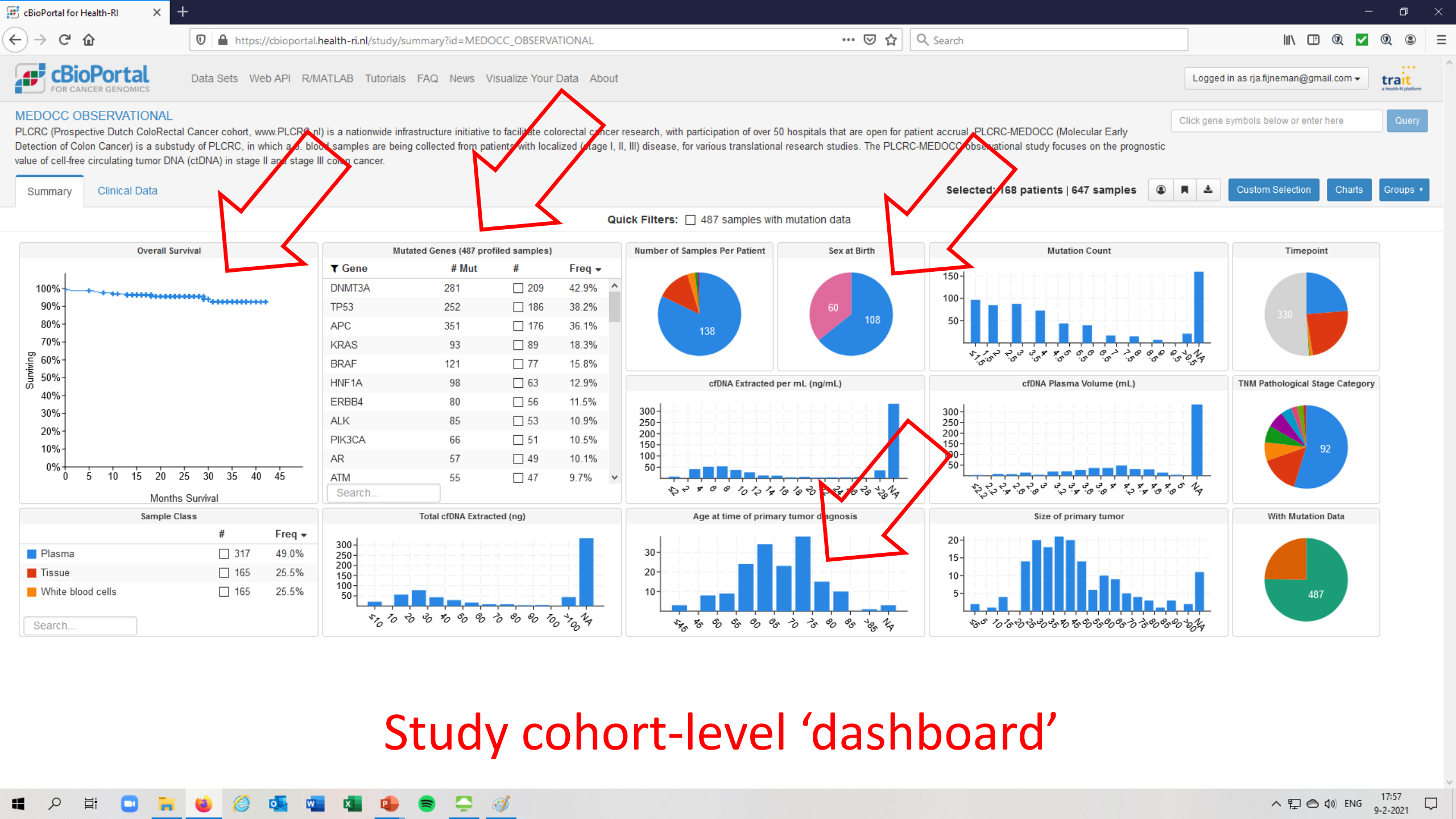
Access to this portal is only available to users authorized by Health-RI. For access to this portal please contact the [Health-RI ServiceDesk](#) or request access [directly](#) (make sure to specify your Google address)

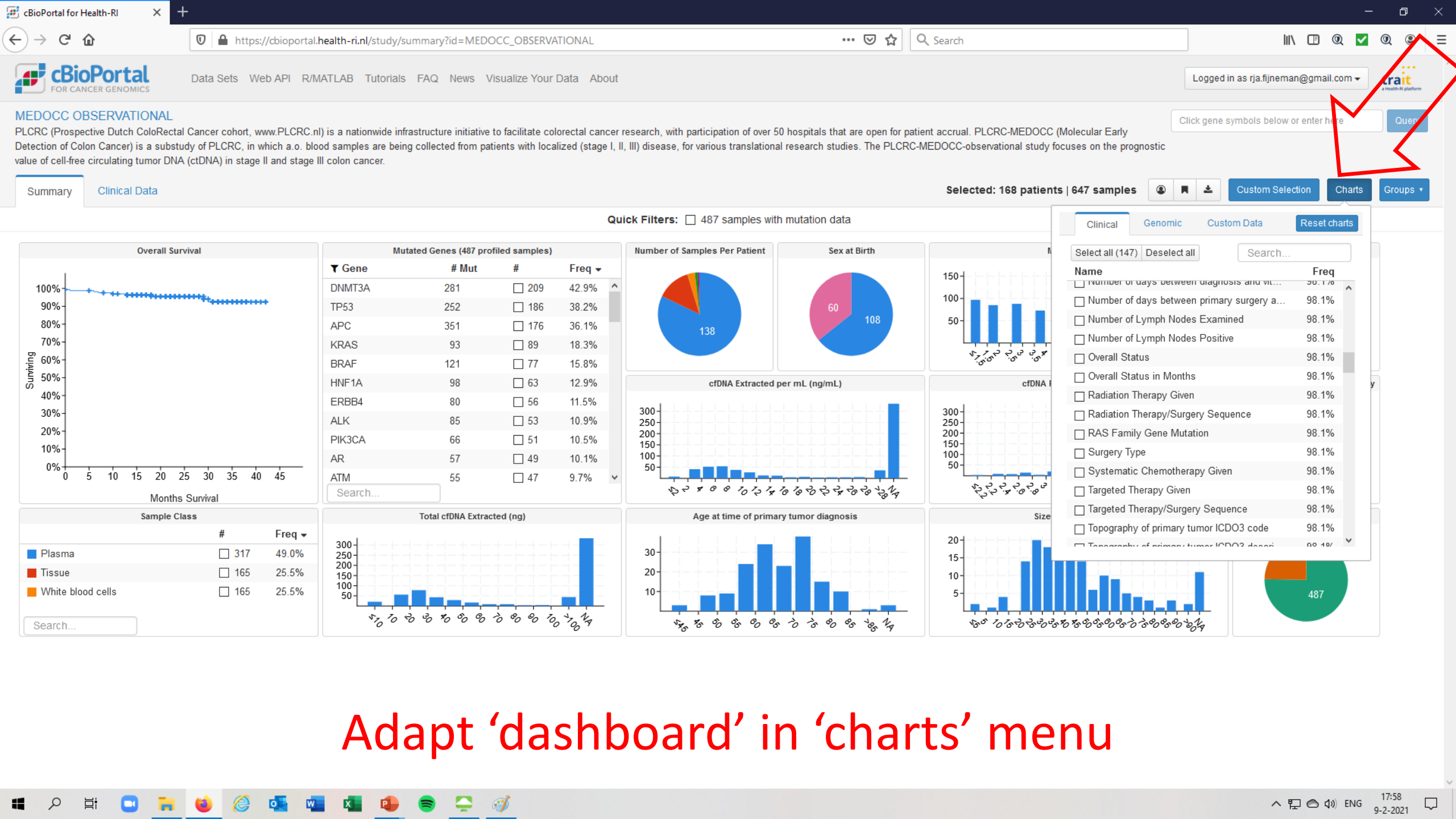


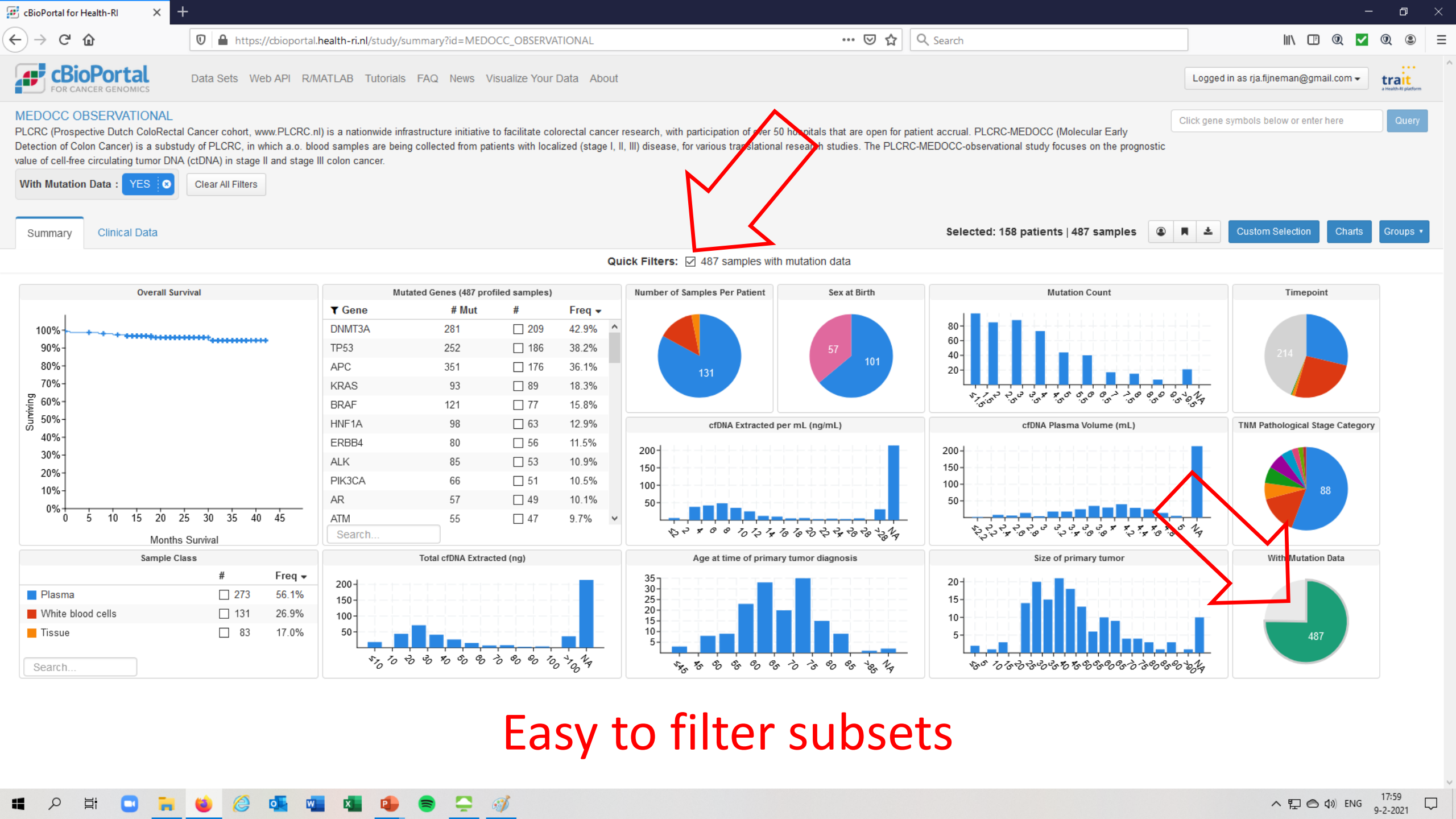
Sign in with
Google credentials

(No, my study
data is **NOT** stored
at Google...)

Disclaimer: MEDOCC use case = Work in progress!







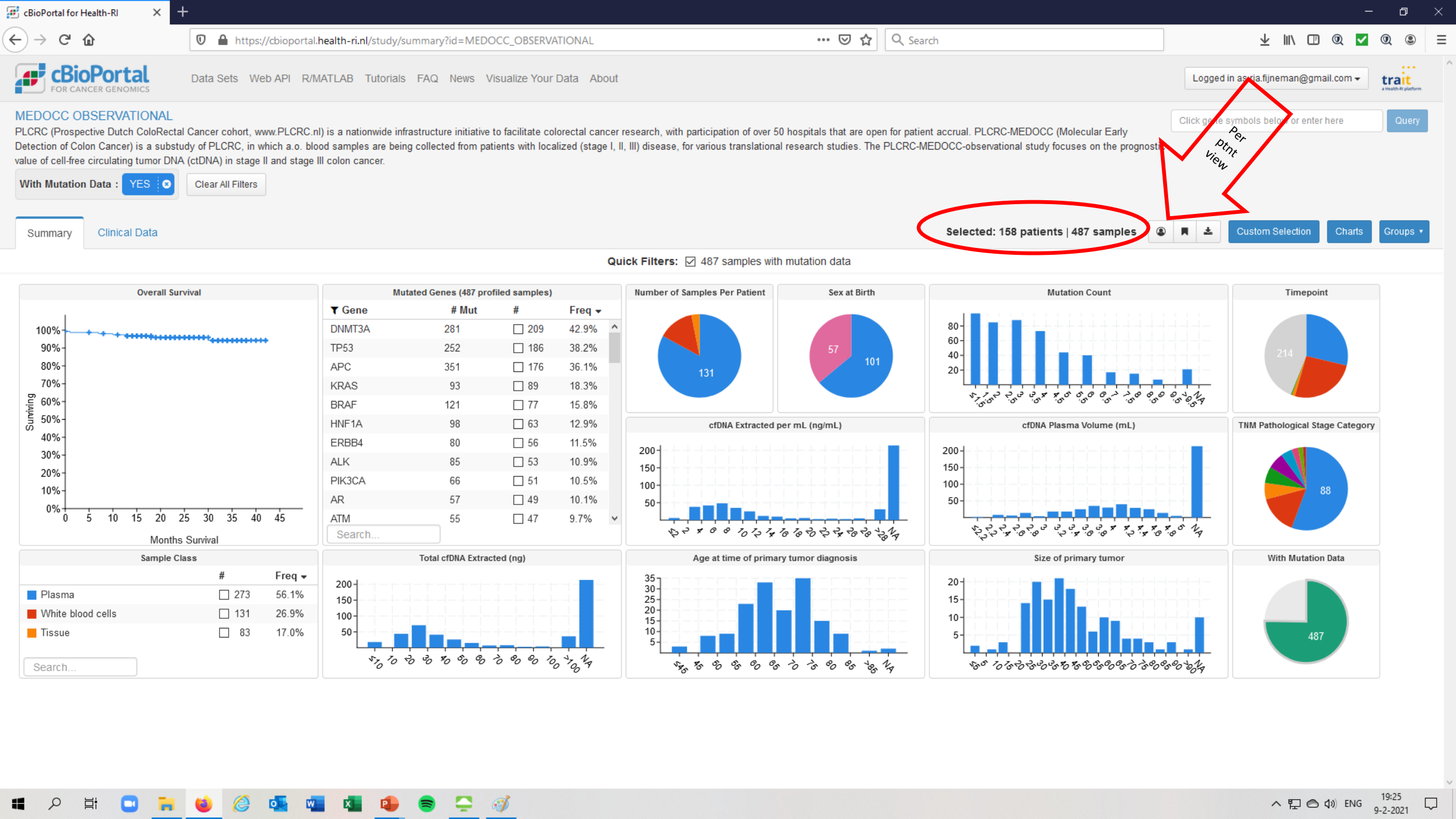
Logged in as rja.fijneman@gmail.com ▼

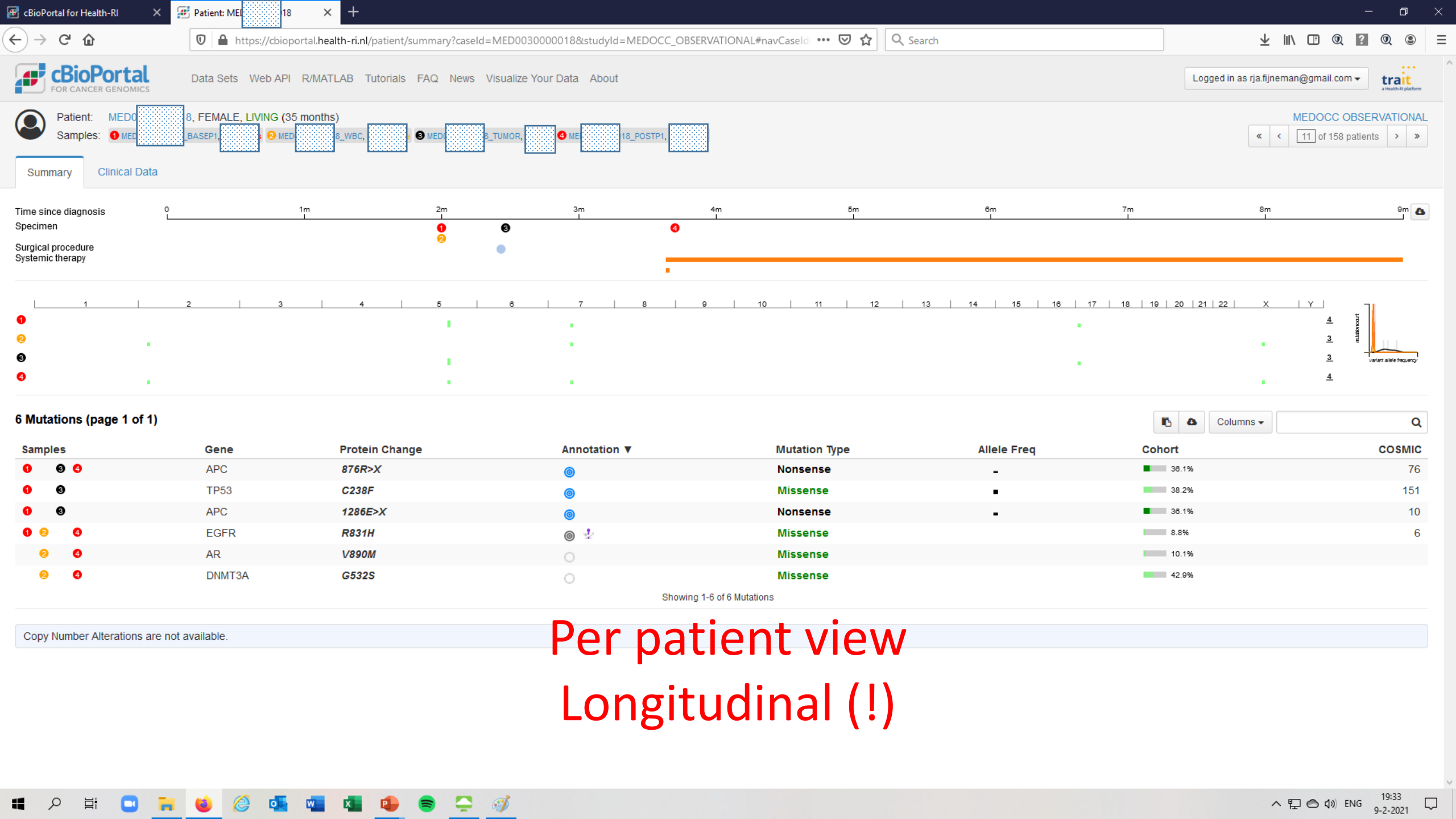
Click gene symbols below or enter here

Selected: 158 patients | 487 samples

Custom Selection Columns Groups ▾

Study cohort clinical data
'like SPSS or Excel sheet'





Per patient view

MEDOCC OBSERVATIONAL

PLCRC (Prospective Dutch ColoRectal Cancer cohort, www.PLCRC.nl) is a nationwide infrastructure initiative to facilitate colorectal cancer research, with participation of over 50 hospitals that are open for patient accrual. PLCRC-MEDOCC (Molecular Early Detection of Colon Cancer) is a substudy of PLCRC, in which a.o. blood samples are being collected from patients with localized (stage I, II, III) disease, for various translational research studies. The PLCRC-MEDOCC-observational study focuses on the prognostic value of cell-free circulating tumor DNA (ctDNA) in stage II and stage III colon cancer.

Custom Selection : 487 samples Sample Class : Tissue [Clear All Filters](#)

Summary Clinical Data

Selected: 83 patients | 83 samples

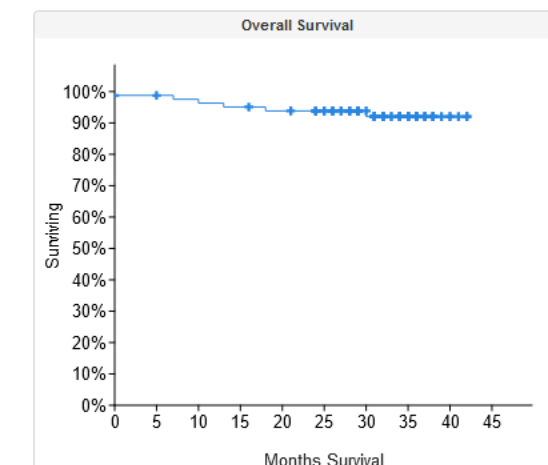


Custom Selection

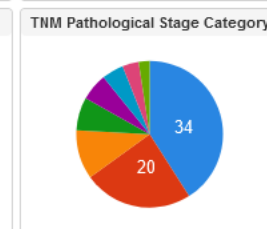
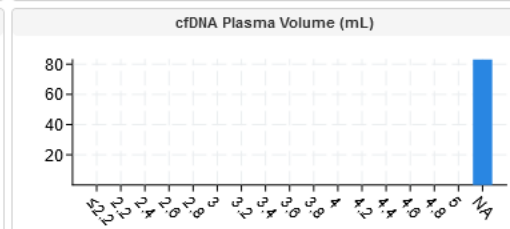
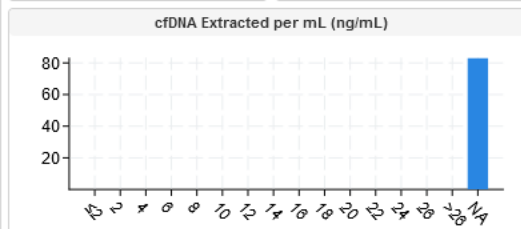
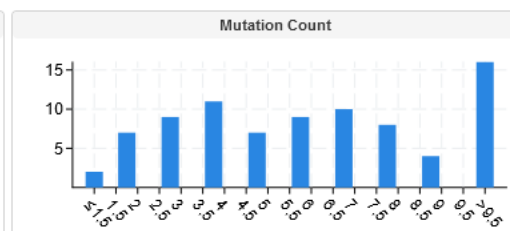
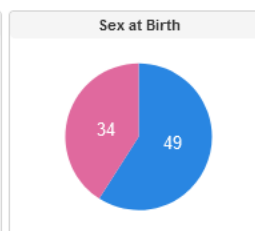
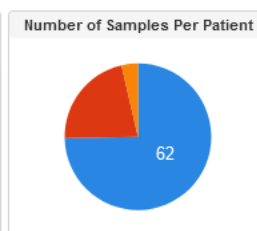
Charts

Groups ▾

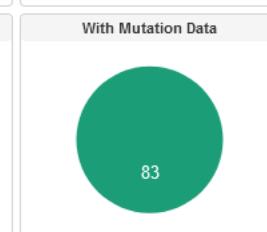
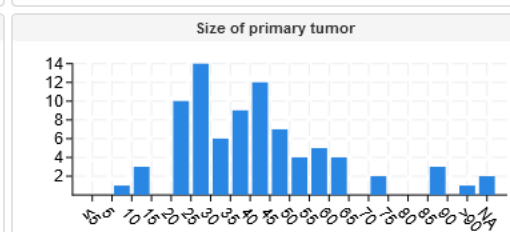
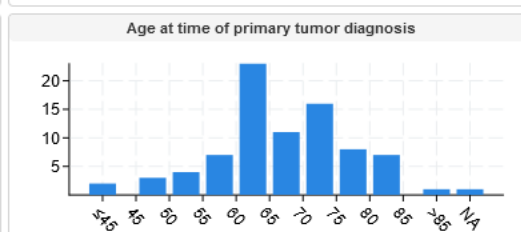
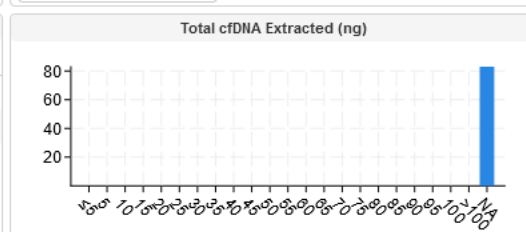
Quick Filters: ☐ 83 samples with mutation data

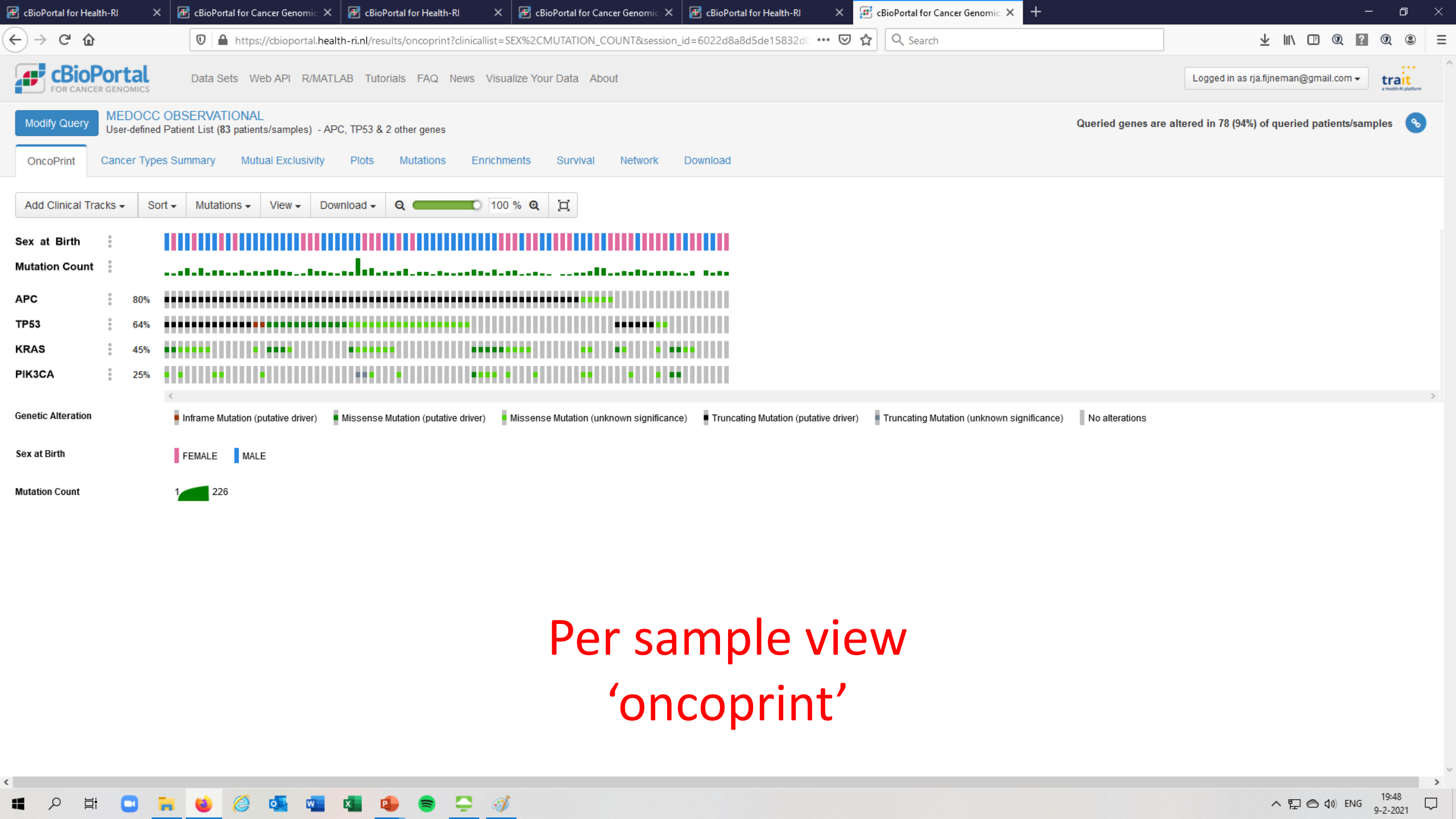


Mutated Genes (83 profiled samples)			
Gene	# Mut	#	Freq
APC	193	66	79.5%
TP53	91	53	63.9%
BRAF	81	42	50.6%
KRAS	40	37	44.6%
PIK3CA	32	21	25.3%
AR	24	16	19.3%
HNF1A	26	16	19.3%
ALK	34	14	16.9%
FBXW7	28	13	15.7%
PTEN	21	11	13.3%
SMAD4	17	10	12.0%



Sample Class		
	#	Freq
<input type="checkbox"/> Plasma	273	56.1%
<input type="checkbox"/> White blood cells	131	26.9%
<input checked="" type="checkbox"/> Tissue	83	17.0%

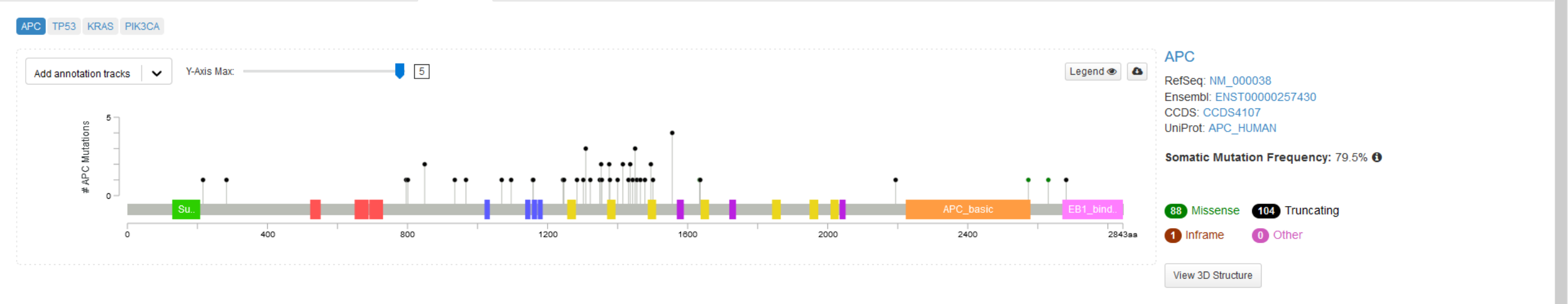




Modify Query MEDOCC OBSERVATIONAL User-defined Patient List (83 patients/samples) - APC, TP53 & 2 other genes

Queried genes are altered in 78 (94%) of queried patients/samples

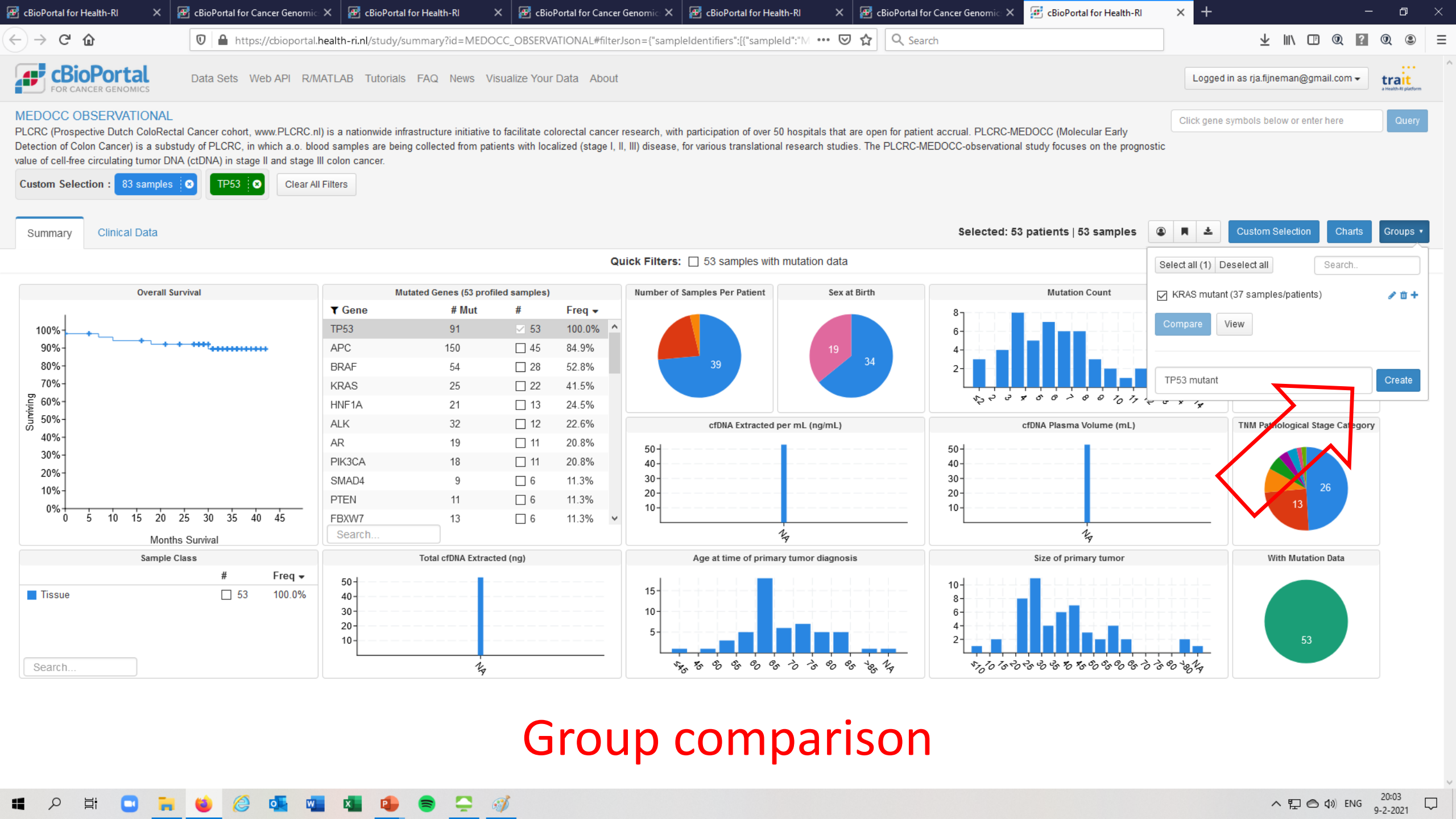
OncoPrint Cancer Types Summary Mutual Exclusivity Plots Mutations Enrichments Survival Network Download

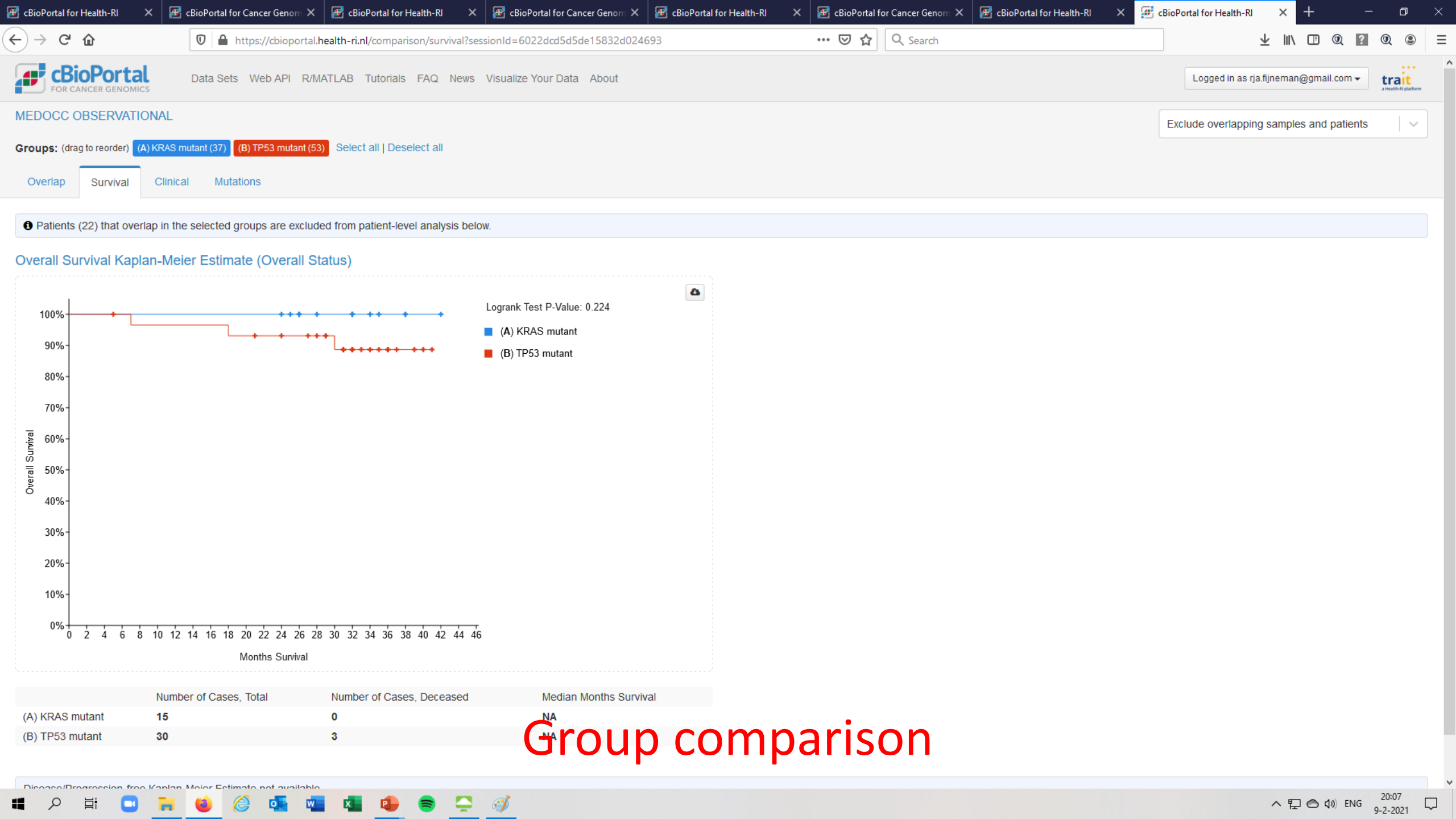


193 Mutations (page 1 of 8)

Sample ID	Protein Change	Annotation	Mutation Type	COSMIC	Allele Freq (T)	# Mut in Sample
MED0049_TU...	S1415Rfs*5		FS ins	16	0.65	5
MED0016_TU...	1114R>X		Nonsense	51	0.29	4
MED0032_TU...	1114R>X		Nonsense	51	0.22	7
MED0014_TU...	1454K>X		Nonsense	2	0.02	11
MED0026_TU...	955E>X		Nonsense		0.46	2
MED0009_TU...	1350K>X		Nonsense	2	0.05	226
MED0021_TU...	V967Cfs*3		FS ins		0.45	1
MED0029_TU...	1935Q>X		Nonsense		0.26	10
MED0032_TU...	1312G>X		Nonsense	33	0.48	7
MED0062_TU...	S1501Lfs*6		FS del	2	0.55	3
MED0028_TU...	S1495Vfs*12		FS del	7	0.33	7

Per gene view
'lollypop'





Getting started

International server:
www.cbioportal.org

Dutch server:
<https://cbioportal.health-ri.nl>

Online tutorials

<https://cbioportal.health-ri.nl/tutorials>

Frequently Asked Questions

<https://cbioportal.health-ri.nl/faq>

Detailed documentation

<https://docs.cbioportal.org/>

Do you want to upload your data?

Send an email to servicedesk@health-ri.nl

They will inform you on the upload procedure.

Overview

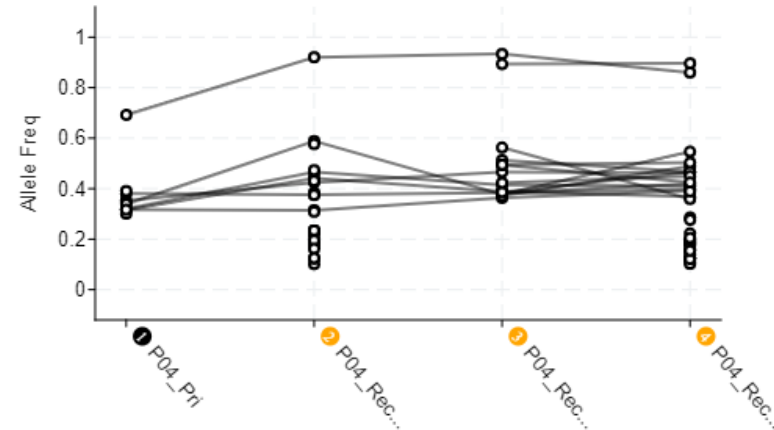
- Position of cBioPortal in the translational research landscape
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cBioPortal – Future perspectives

- Software development cBioPortal community – in progress
 - cBioPortal integration with digital pathology and with clinical imaging
 - Visualization of longitudinal ctDNA data



Digital Pathology
(Jan Hudecek)



A function to incorporate molecular results from
ctDNA analysis is under-development

cBioPortal – Future perspectives??

- Translational research – *multicenter consortia*
 - Automated data flows
 - Clinical data (Netherlands Cancer Registry => cBioPortal)
 - Pathology data (PALGA => cBioPortal)
 - Biobanking data (LMS => cBioPortal)
 - Molecular data (Molecular Diagnostics => cBioPortal)
 - Publications – publish your study in cBioPortal in the public domain
- Clinical setting – *local cBioPortal*
 - Automated data flows => local cBioPortal
 - Molecular Tumor Board => discuss patient in multidisciplinary meeting
 - Federated data access to ‘local cBioPortals’?

Tools themselves are not all that important

What is important: FAIR data!
(however, tools help to en

acknowledgements

Findable
Accessible
Interoperable
Reusable

Gerrit
Meijer



Mariska
Bierkens



GOVERNMENT CENTER
GREEN LINE - NORTH STATION & NORTH

Tools themselves are not all that important
What is important: FAIR data!
(however, tools help to en

acknowledgements

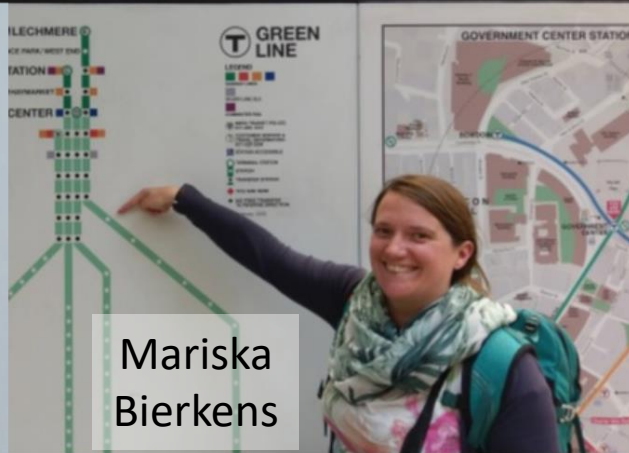
Findable
Accessible
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Gerrit
Meijer



Mariska
Bierkens



Lana Meiqari



Menno de Vries



Brenda Hijmans



Geraldine Vink



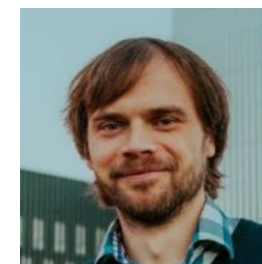
Rita Azevedo



Jan-Willem Boiten



Noriko Cassman



Jan Hudecek



PROSPECTIEF
LANDELIJK
CRC COHORT

Tools themselves are not all that important
 What is important: FAIR data!
 (however, tools help to en



Ino de Bruijn



JJ Gao



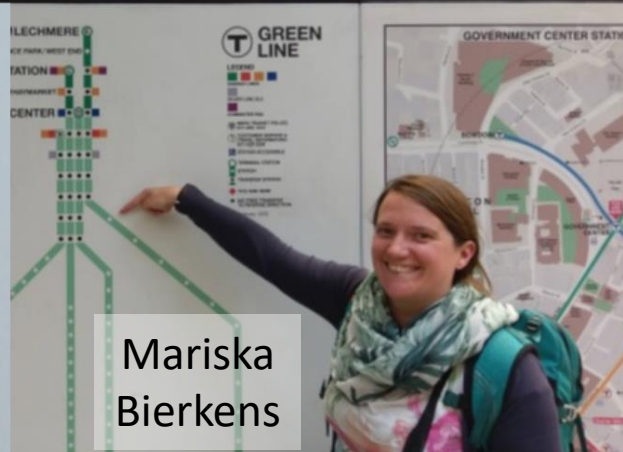
Niki Schultz

Findable
Accessible
Interoperable
Reusable

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Gerrit
Meijer



Mariska
Bierkens



Lana Meiqari



Menno de Vries



Brenda Hijmans

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 CRC COHORT



Geraldine Vink



Rita Azevedo



Jan-Willem Boiten



Noriko Cassman



Jan Hudecek



Questions?

