



Correspondence Problems in Multi-omic data

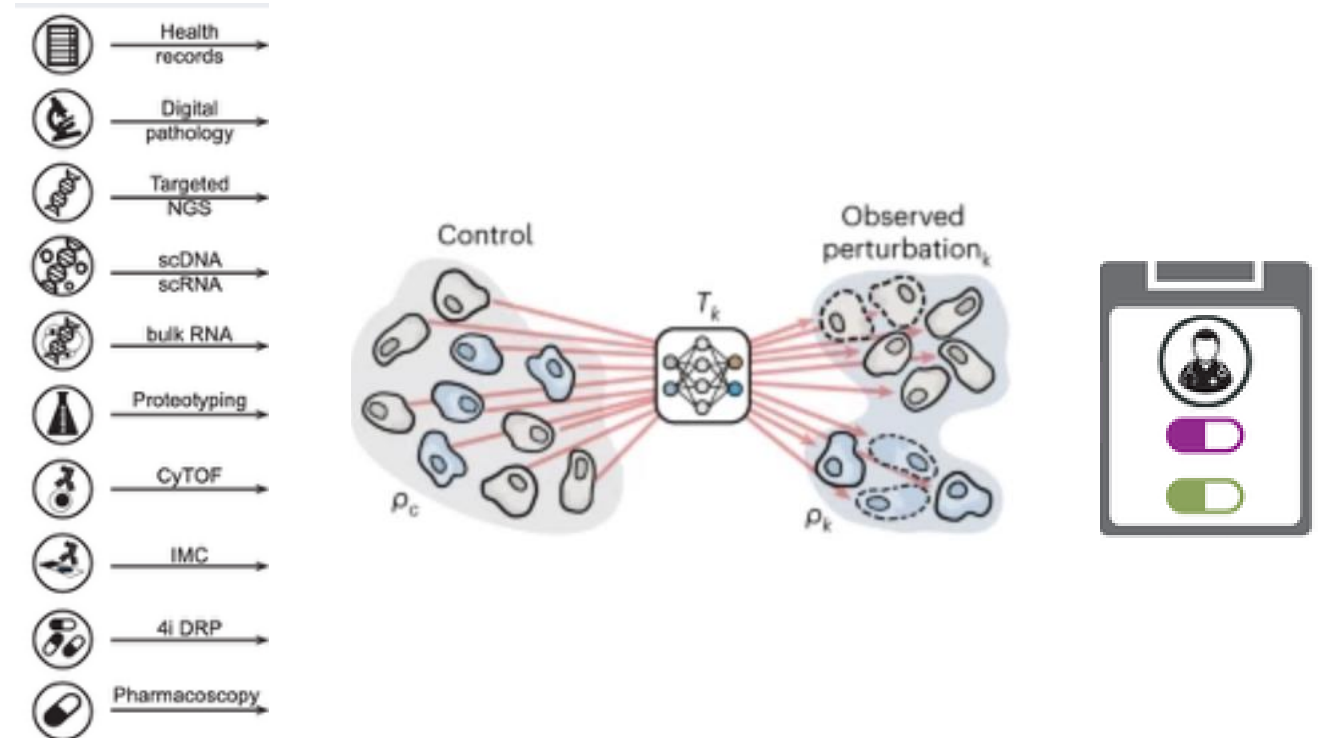
Kjong-Van Lehmann, Ph.D.

kjong.lehmann@rwth-aachen.de

Machine Learning in Cancer Genetics and Precision Medicine
RWTH Aachen and Uniklinik RWTH Aachen

Digital Twin for molecular state changes of cancer (Horizon Mission Cancer Call)

- Build this around perturbation model but make it accessible for routine diagnostics
 - Ovarian Cancer mostly lethal
 - ~70% diagnosed late
 - Uncertain origin
 - No reliable tumor marker
 - Fast progression
 - Chemotherapy currently standard treatment
 - More treatments do become available but choices to be made!



Pretty much everything still needed.

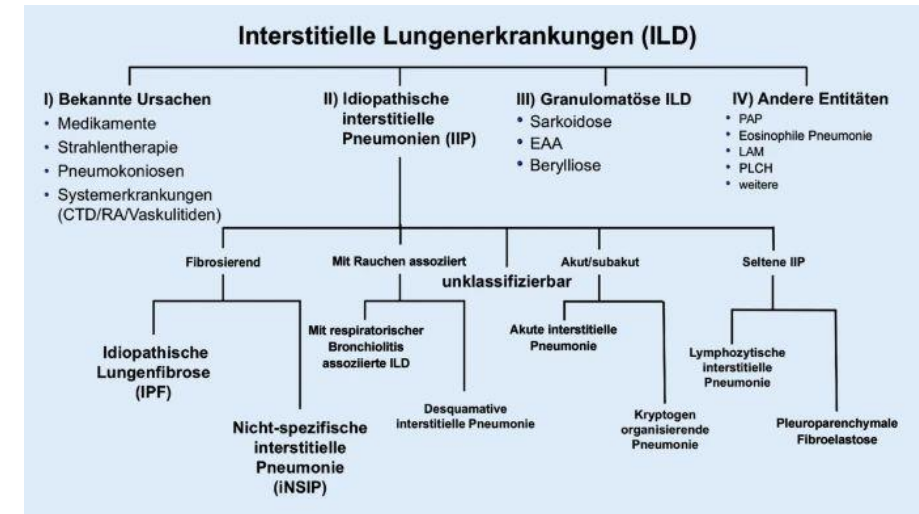
- We have potential partners in Ovarian Cancer and some appropriate data (more the merrier though!)
- Computational and Biomedical experts specialized on various technologies
- Oncological View and relevance
- Access to more cohorts and data.

Digital Twin in Interstitial Lung Disease (Fibrosis)

- Heterogeneous set of diseases
- Various etiologies
- Group of idiopathic of particular interest, since difficult to treat.

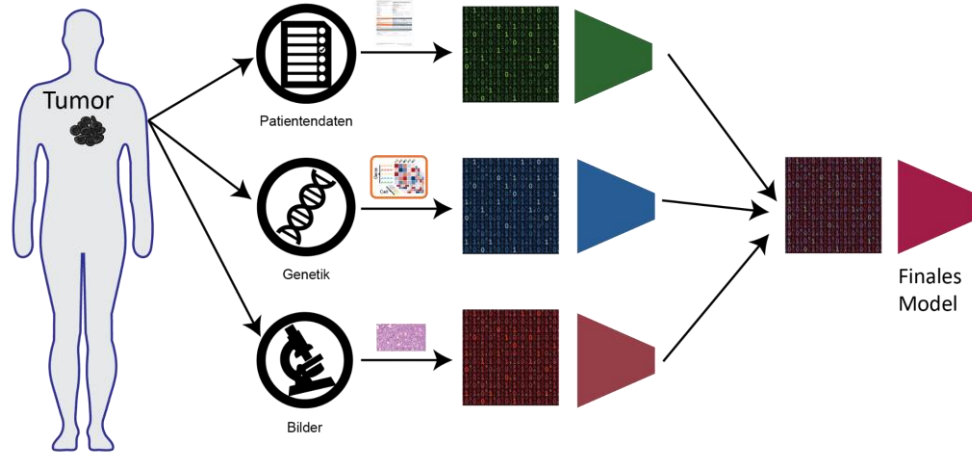
Expertises and Data needed

Expert in Pneumology possibly already on board



Longitudinal Model to find good intervention moments pre-trained on research data

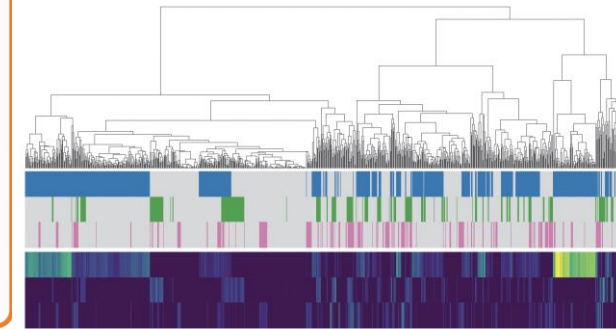
Multimodal Integration (Technical Projects)



Complex Biomarker (Question Driven / Analysis)

A Mutational signatures useful in analysis						B Underlying mutational process	C Relevant genes	D Predisposition syndrome	E Proposed therapy choice
CS-3	CS-8	MH-indels	RS-3	RS-5	HRD index	Homologous Recombination Repair Deficiency	BRCA1, BRCA2, RAD51G, PALB2	Hereditary Breast and Ovarian Cancer Syndrome	PARP inhibition ¹²⁻¹⁴ Platinum-based chemotherapy ¹⁵⁻¹⁷
CS-6	CS-15	CS-20	CS-26	STR-indels		Mismatch Repair Deficiency	MLH1, MSH2, MSH6, PMS1, PMS2	Lynch, CMMRD, BMMR-D, HNPCC	PD1-immunotherapy ^{18,19,21}
CS-5	CS-8	TSB-sign				Nucleotide Excision Repair Deficiency	ERCC1, ERCC2, XPC	Xeroderma Pigmentosum	Cisplatin ²²⁻²⁵
CS-18	CS-30	TSB-sign	C>A*	G>T*	C>T*	Base excision Repair Deficiency	MUTYLOGG1	MAP	
CS-10	STR-indels					Deficient DNA polymerase proofreading activity	POLE, POLD1	PPAP	PD1-immunotherapy ^{18,19,21}
?						Non-Homologous End Joining Deficiency		Nijmegen Breakage Syndrome	
CS-2	CS-13	Exonops				APOBEC Over-activity	APOBEC1, APOBEC2A, APOBEC2B		Tamoxifen Resistance ^{26,27}

A. Van Hoeck, BMC Cancer 2019



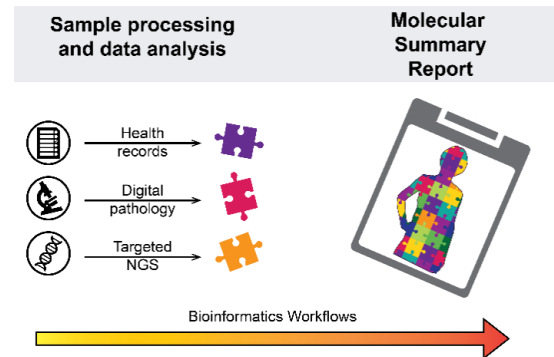
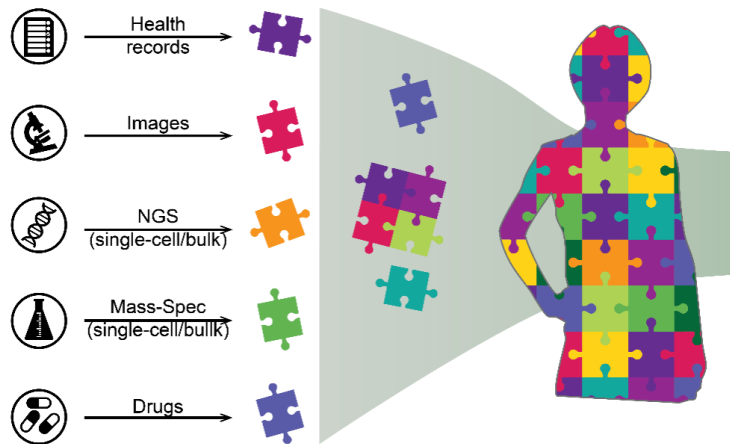
A. Immer ... KV. Lehmann Bioinformatics 2024
 C. Bunne ... KV. Lehmann*, L. Pelkmans*, A. Krause*, G. Rätsch*, Nature Methods, 2023
 S. Stark ... KV. Lehmann Bioinformatics 2020
 X. Liu ... KV. Lehmann Bioinformatics 2020





Thank you for your attention!

kjong.lehmann@rwth-aachen.de



Centrum für Integrierte Onkologie
Aachen Bonn Köln Düsseldorf

