

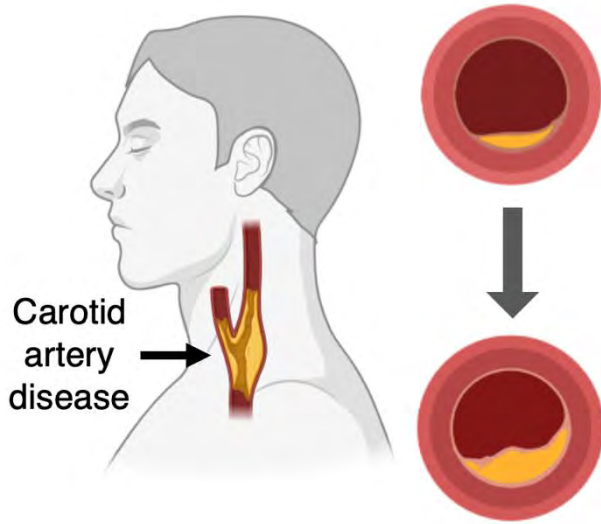
# Deciphering human atherosclerosis with multi-omics

Univ.-Prof. Dr. med. Lars Maegdefessel

DigiMed Bayern

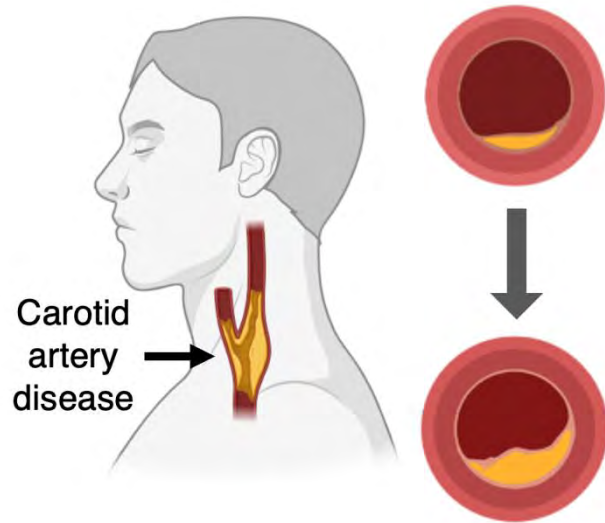
Work package 2 on P-4 medicine in carotid artery disease and stroke

# Carotid artery disease and stroke

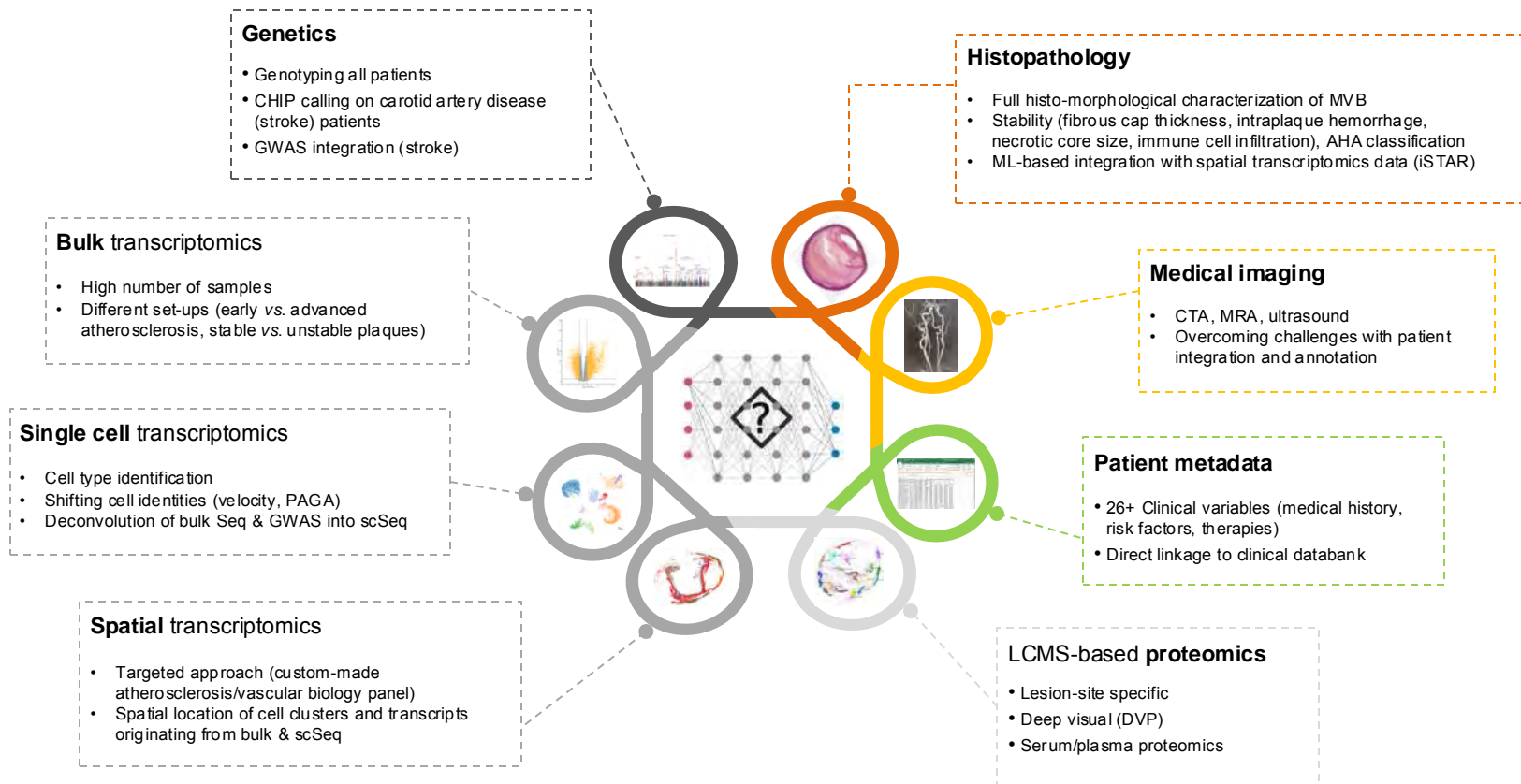


- 12.2M strokes/year worldwide
- 1 in 4 people will suffer from stroke in their lifetime
- 89% of global stroke deaths & disability reside in low/middle-income countries
- Up to 80% of strokes occur in people with low-moderate CV risk
- Total estimated global stroke cost/year is \$450B (0.36 of global GDP)

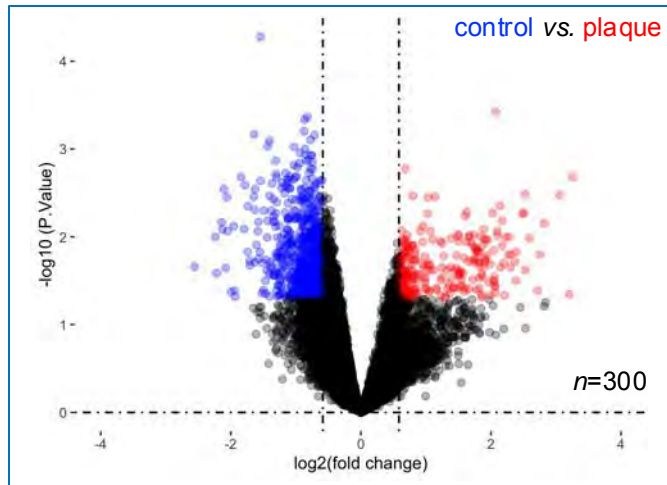
# Carotid artery disease and stroke



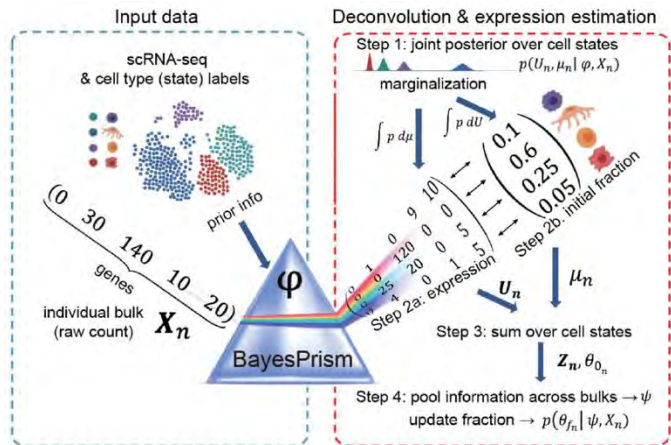
# Profiling atherosclerosis with human plaque biobanks



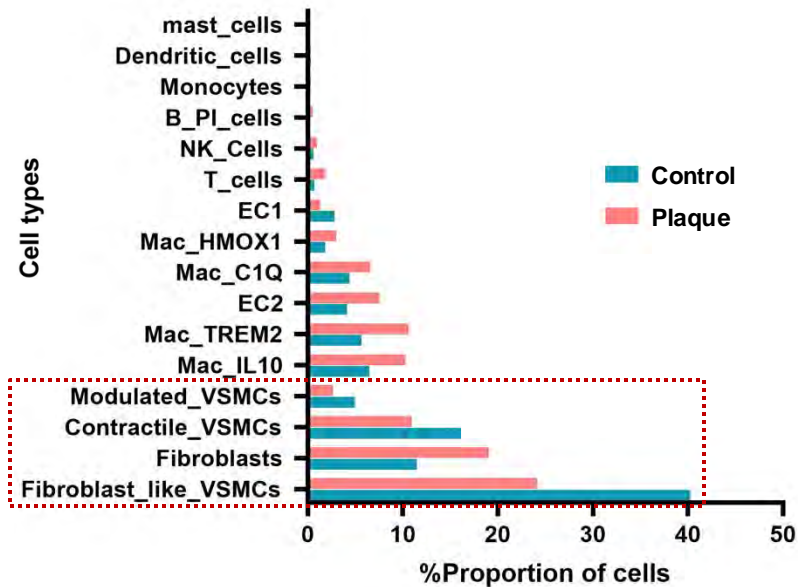
# Bulk and scRNA-Seq of human plaques



# Single cell and bulk RNA-Seq deconvolution



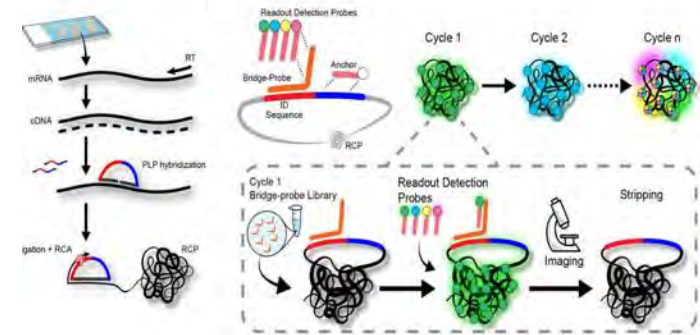
[www.bayesprism.org](http://www.bayesprism.org)  
 Chu T, *Nat Cancer* 2022



# Targeted spatial transcriptomics

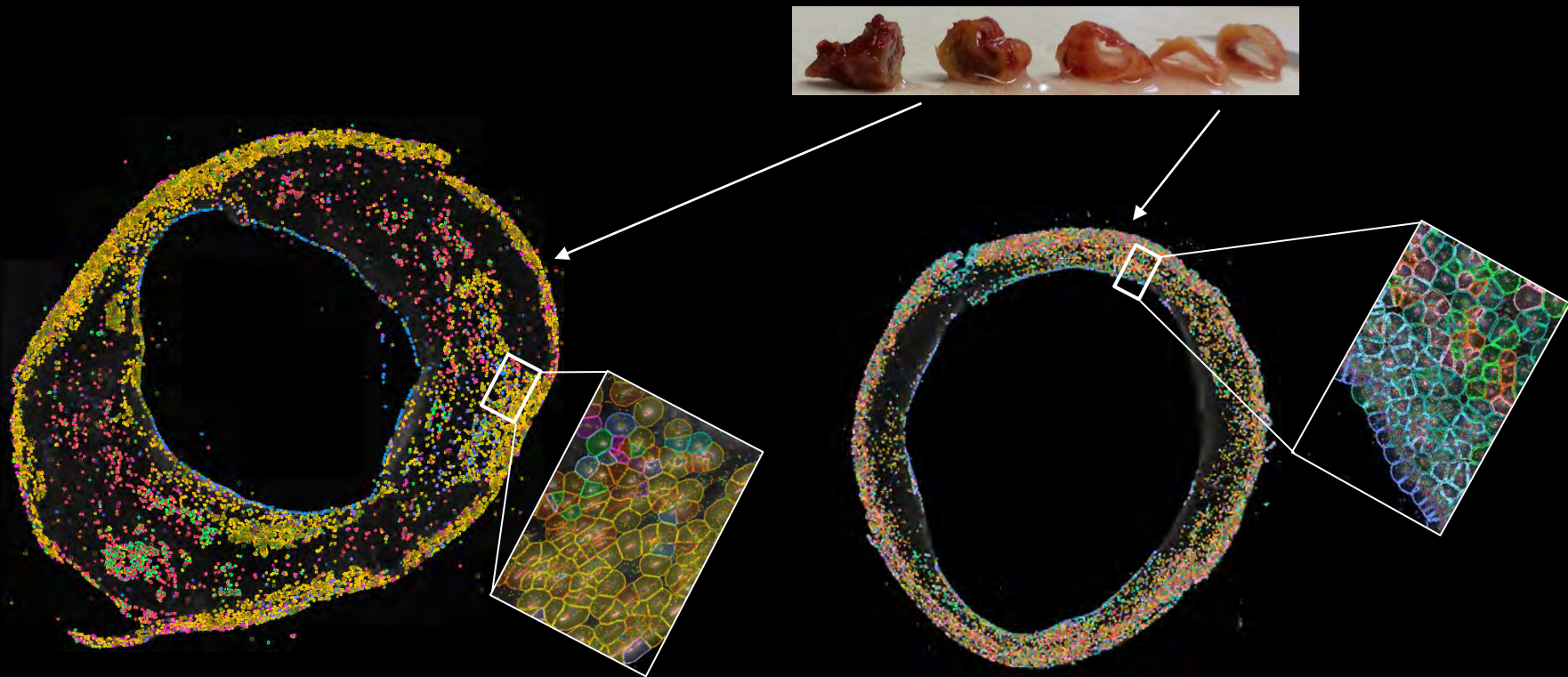


## Hybridization-based RNA In Situ Sequencing



Le Manno G *et al*, *Nature* 2021

# Targeted spatial transcriptomics in human atherosclerosis





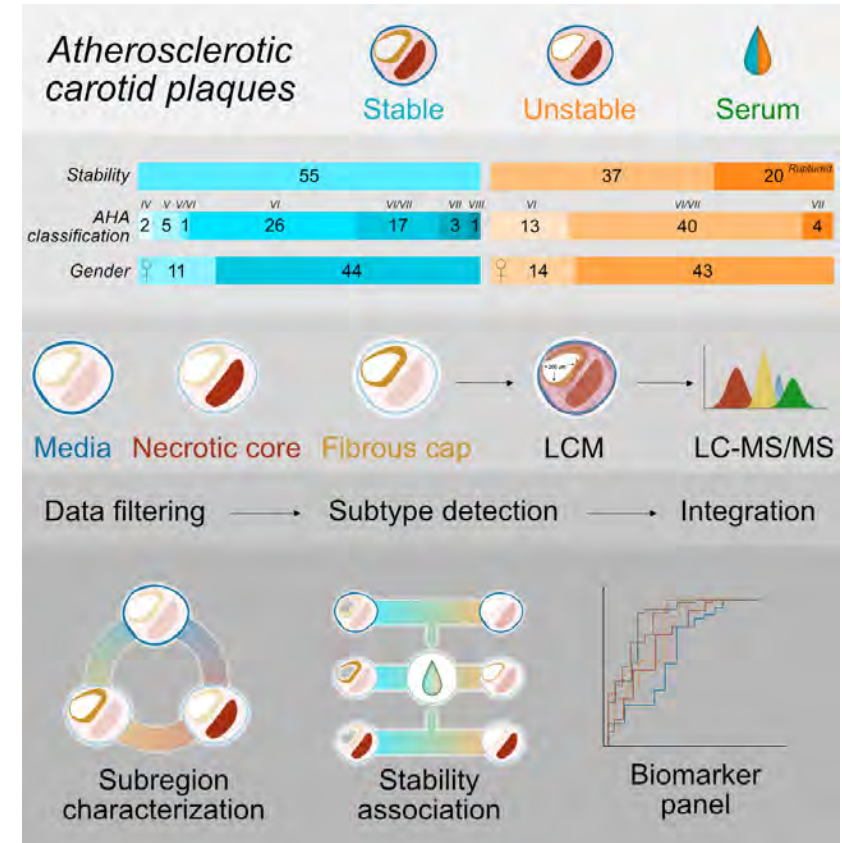
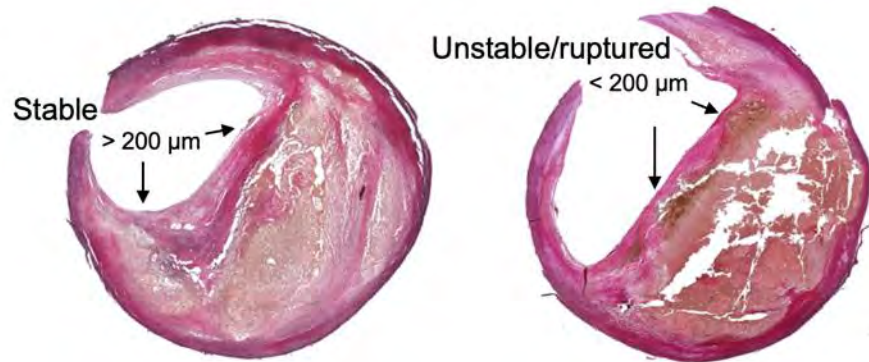


**AI-guided detection of atherosclerotic plaque instability**

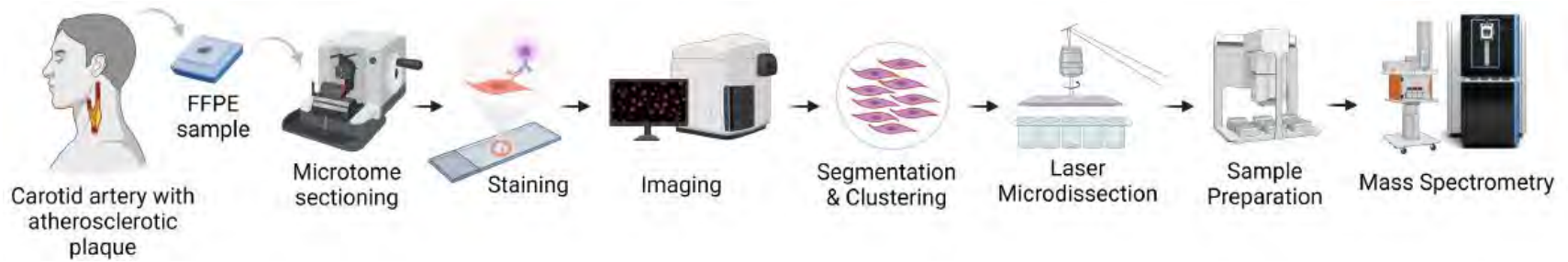
Combining plaque histomorphology with unsupervised patient information to determine features of lesion destabilization

*in collaboration with Mingyao Li (UPenn) & Muredach Reilly (Columbia)*

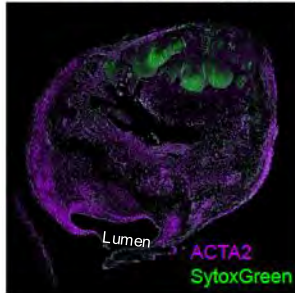
# Proteomic profiling of plaque vulnerability



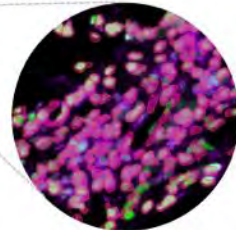
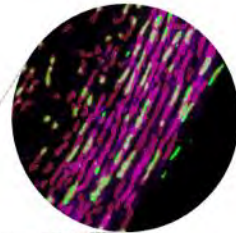
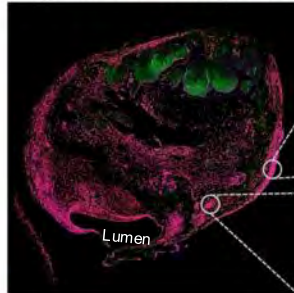
# Deep visual proteomics (DVP) in atherosclerosis



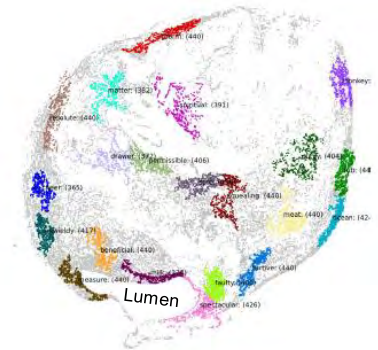
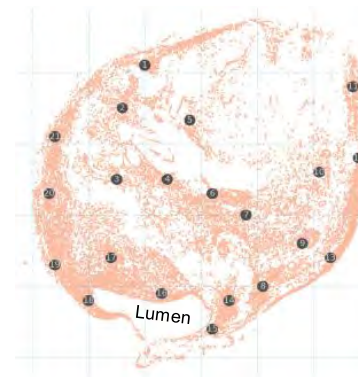
Staining



Segmentation



Density-based clustering of 21 spatial neighborhoods



# Conclusions

- Multi-omics identifies novel processes relevant to plaque vulnerability
- (Vascular) smooth muscle cells are the most abundant cell type in atherosclerotic lesions
- Smooth muscle cell profile and plasticity differs based on spatial location in plaques
- Changes in the necrotic core proteome are the strongest determinators of plaque stability

# Acknowledgement



Valentina Paloschi, Francesca Fasolo, Nadja Sachs, Hanna Winter, Jessica Pauli, Nadiya Glukha, Julia Ritzer, Zhaolong Li, Trusha Adeshara, Justus Wettig, Katrin Hanft, Annalena Huber, Renate Hegenloh, Thomas Scherbauer, Katja Chernogubova, Hong Jin, Greg Winski, Felix Kirchhoff, Joscha Büch & Coco

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Daniela Branzan & team (TUM-Vascular Surgery)  
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Ankit Sinha, Elena Kratz, Matthias Mann (MPI, Martinsried)  
Ulf Hedin, Ljubica Matic (Karolinska)  
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Muredach Reilly (Columbia)  
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