北京大学肿瘤医院
BEIJING CANCER HOSPITAL

Proteogenomic Characterization of Human Gastric Cancer

Presenter: **Yang Du,** Ph. D.

Center for Cancer Bioinformatics

Peking University Cancer Hospital & Institute

Jianmin Wu [1] , Ludovic Gillet [2] , Tiannan Guo [2 3] , **Yang Du** [1] , Sijia Cui [1] , Luxi Zhang [1] , Huan Yu [1] , Lihua Cao [1] , Peng Xue [2 4] , Yi Zhu [2 3] , Yang Yang [1] , Man Wang [1] , Xiaoqing Guan [1] , Bin Dong [1] , Ying Hu [1] , Xiaofang Xing [1] , Xiangyu Gao [1] , Fei Shan [1] , Lei Tang [1] , Lianhai Zhang [1] , Zhongwu Li [1] , Xiangqian Su [1] , Aiwen Wu [1] , Zhaode Bu [1] , Ziyu Li [1] , Shuqin Jia [1] , Ruedi Aebersold [2 5] , Jiafu Ji [1]

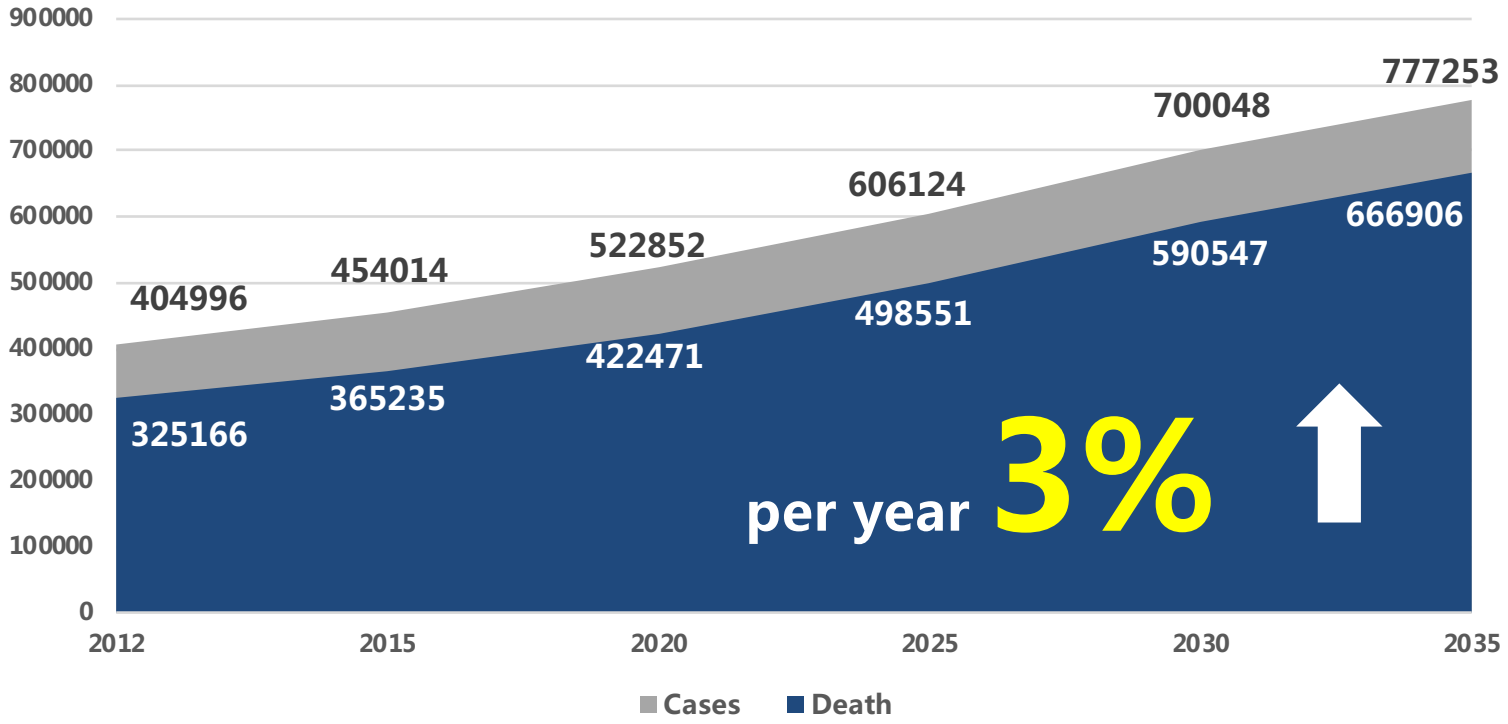
1. Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Peking University Cancer Hospital & Institute, Beijing, China
2. Department of Biology, Institute of Molecular Systems Biology, ETH Zurich, Zurich, Switzerland
3. School of Life Sciences, Westlake University, Hangzhou, Zhejiang Province, China
4. Institue of biophysics, Chinese academy of science, Beijing, China
5. Faculty of Science , University of Zurich, Zurich, Switzerland

Adelaide, 18th Sep 2019

Chinese Gastric Cancer Stats

北京大学肿瘤医院
BEIJING CANCER HOSPITAL

2035 New Cases **770 k** / **670 k** Cancer Death



42.5%
News cases worldwide

80%
Diagnosis at Advanced stage

Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://globocan.iarc.fr, accessed on day/month/year.

Clinical trials in Gastric Cancer (GC)

北京大学肿瘤医院 BEIJING CANCER HOSPITAL

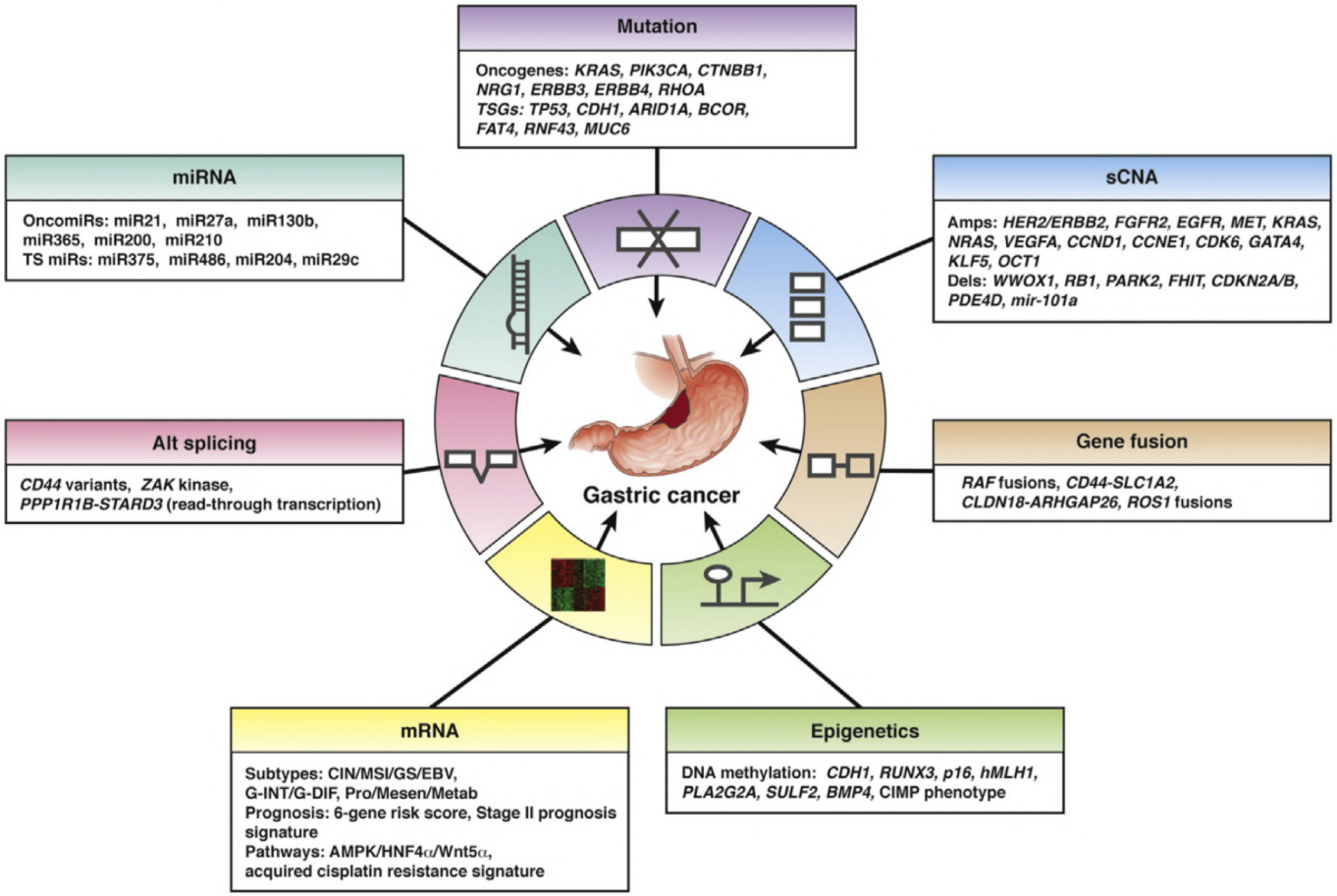
Table 1 Recent phase 3 of new agents for GC

Target	Trial/author	Line	Screening	Agent	Control	Endpoint	Result	Difference mOS (m) (HR)
HER2	ToGA	1st	HER2	Trastuzumab	(+chemo)	OS	Positive	+2.7 (HR 0.74)
HER2	Logic	1st	HER2 (FISH)	Lapatinib	PBO (+chemo)	OS	Negative	+1.7 (HR 0.91)
HER2	JACOB	1st	HER2	Pertuzumab	PBO (+chemo + Tmab)	OS	Negative	+3.3 (HR 0.84)
HER2	TyTAN	2nd	HER2 (FISH)	Lapatinib	(+chemo)	OS	Negative	+3 (HR 0.84)
HER2	GATSBY	2nd	HER2	T-DM1	Taxanes	OS	Negative	−0.7 (HR 1.15)
EGFR	REAL-3	1st	–	Panitumumab	(+chemo)	OS	Negative	−2.5 (HR 1.37)
EGFR	EXPAND	1st	–	Cetuximab	PBO (+chemo)	PFS	Negative	−1.3 (HR 1.0)
EGFR	ENRICH	2nd	EGFR (IHC)	Nimotuzumab	(+chemo)	OS	Negative	
mTOR	GRANITE-1	2nd/3rd	–	Everolimus	PBO	OS	Negative	+1.05 (HR 0.9)
mTOR	GRANITE-2	2nd	–	Everolimus	PBO (+chemo)	OS	Negative	+1.0 (HR 0.92)
HGF	RILOMET1	1st	MET (IHC)	Rilotumumab	PBO (+chemo)	OS	Negative	−2.9 (HR 1.36)
MET	METgastric	1st	MET (IHC)	Onartuzumab	PBO (+chemo)	OS	Negative	−0.3 (HR 0.82)
VEGF-A	AVAGAST	1st	–	Bevacizumab	PBO (+chemo)	OS	Negative	+2 (HR 0.87)
VEGFR2	RAINFALL	1st	–	Ramucirumab	PBO (+chemo)	OS	Negative	+0.4 (HR 0.96)
VEGFR2	REGARD	2nd	–	Ramucirumab	PBO	OS	Positive	+1.4 (HR 0.776)
VEGFR2	RAINBOW	2nd	–	Ramucirumab	PBO (+chemo)	OS	Positive	+2.2 (HR 0.807)
VEGFR2	Li. et al.	3rd	–	Apatinib	PBO	OS	Positive	+1.8 (HR 0.71)
PARP	GOLD	2nd	ATM (IHC)	Olaparib	PBO (+chemo)	OS	Negative	+1.9 (HR 0.79)
STAT3	BRIGHTER	2nd	–	Napabucasin	PBO (+chemo)	OS	Negative	−0.4 (HR 1.01)
PD1	Keynote061	2nd	PD-L1 (IHC)	Pembrolizumab	Paclitaxel	OS	Negative	+0.8 (HR 0.82)
PD1	JAVELIN300	3rd	–	Avelumab	Irinotecan/taxanes/BSC	OS	Negative	−0.4 (HR 1.1)
PD1	ATTRACTION-2	3rd	–	Nivolumab	PBO	OS	Positive	+1.2 (HR 0.63)

PBO placebo

Ishii T., Kawazoe A., Shitara K. International Journal of Clinical Oncology, 2019

Current understanding of GC Genomics



GC patients can benefit from current genomic knowledge is about 20%

Tan P., Yeoh K.G. *Gastroenterology* 2015

Proteogenomic studies focused on diffuse GC

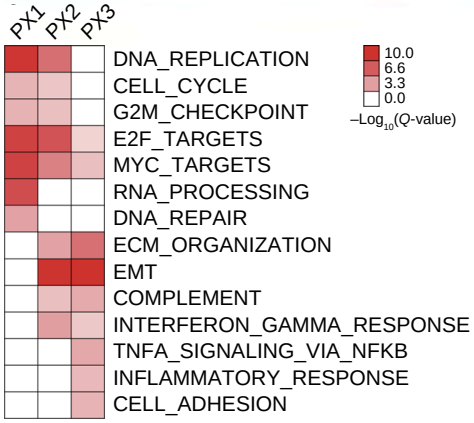
北京大学肿瘤医院
BEIJING CANCER HOSPITAL

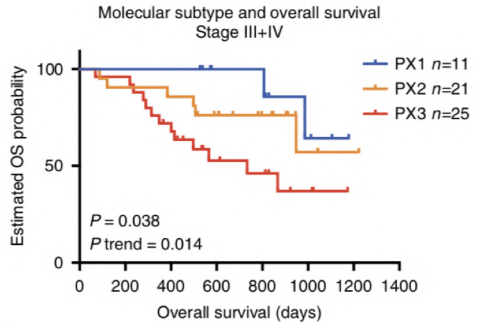
DOI: 10.1038/s41467-018-03121-2 OPEN

A proteomic landscape of diffuse-type gastric cancer

Sai Ge[1,2], Xia Xia[1], Chen Ding[1,3], Bei Zhen[1], Quan Zhou[1], Jinwen Feng[1,4], Jiajia Yuan[1,2], Rui Chen[5], Yumei Li[5], Zhongqi Ge[5], Jiafu Ji[2], Lianhai Zhang[2], Jiayuan Wang[2], Zhongwu Li[2], Yumei Lai[2], Ying Hu[2], Yanyan Li[2], Yilin Li[2], Jing Gao[2], Lin Chen[6], Jianming Xu[7], Chunchao Zhang[8], Sung Yun Jung[8], Jong Min Choi[8], Antrix Jain[8], Mingwei Liu[1], Lei Song[1], Wanlin Liu[1], Gaigai Guo[1], Tongqing Gong[1], Yin Huang[1], Yang Qiu[1], Wenwen Huang[1,2], Tieliu Shi[4], Weimin Zhu[1], Yi Wang[1,8], Fuchu He[1,3], Lin Shen[1,2] & Jun Qin[1,3,8]

- **84 diffuse GCs** with paired normal



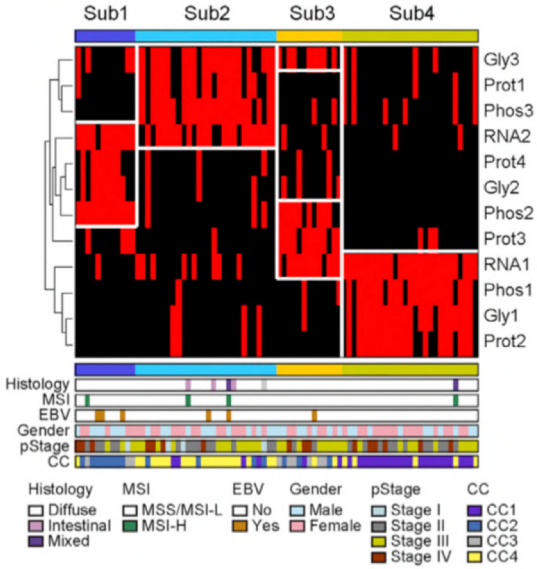


Cancer Cell
Article

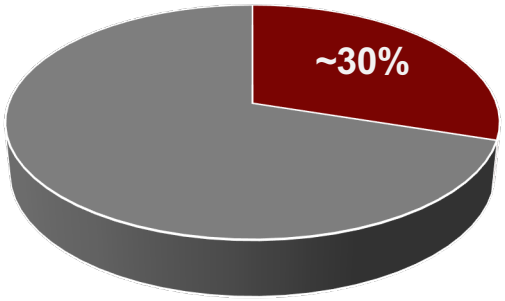
Proteogenomic Characterization of Human Early-Onset Gastric Cancer

Dong-Gi Mun,[1,21] Jinhyuk Bhin,[2,3,21] Sangok Kim,[4,21] Hyunwoo Kim,[5,6,21] Jae Hun Jung,[7,21] Yeonjoo Jung,[4] Ye Eun Jang,[4] Jong Moon Park,[8] Hokeun Kim,[1] Yeonhwa Jung,[4] Hangyeore Lee,[1] Jingi Bae,[1] Seunghoon Back,[1] Su-Jin Kim,[1] Jieun Kim,[4] Heejin Park,[5] Honglan Li,[9] Kyu-Baek Hwang,[9] Young Soo Park,[10] Jeong Hwan Yook,[11] Byung Sik Kim,[11] Sun Young Kwon,[12] Seung Wan Ryu,[12] Do Youn Park,[13] Tae Yong Jeon,[14] Dae Hwan Kim,[14]

- **74 diffuse GCs**, 6 other GCs of Early-Onset



Gastric Cancer

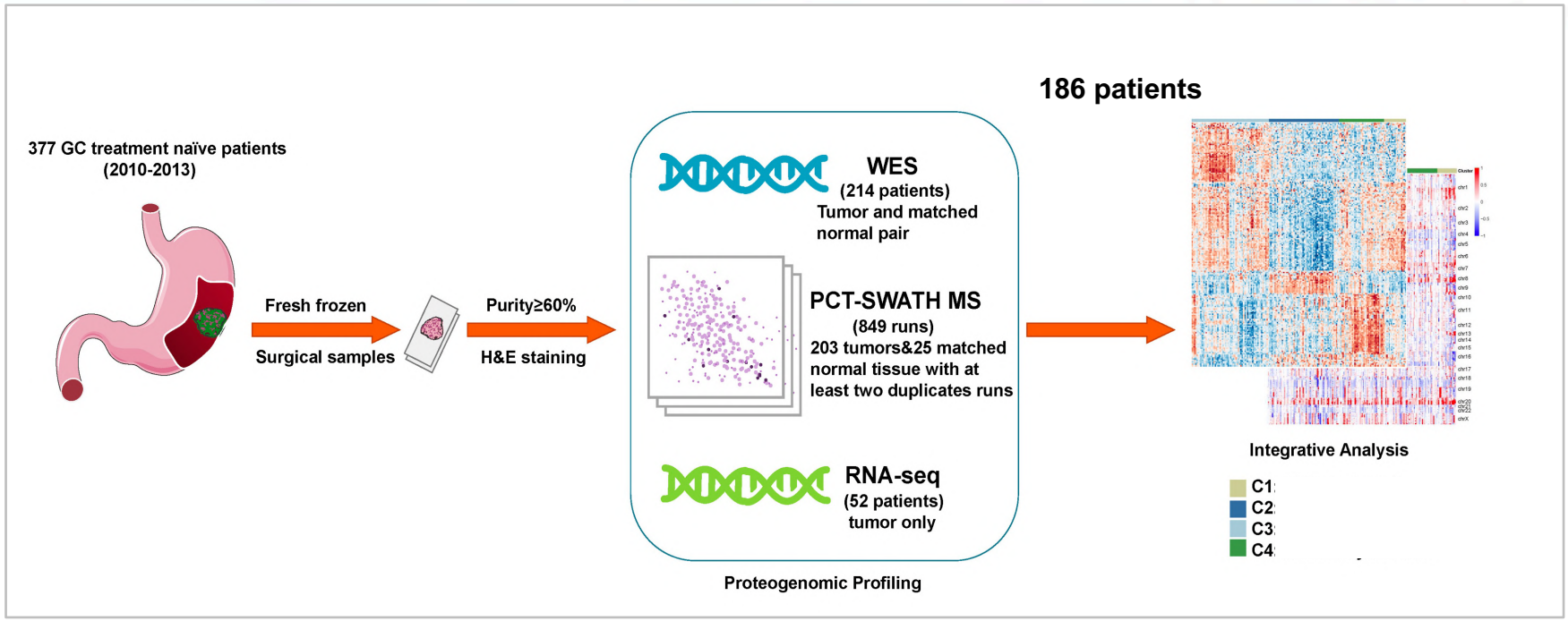


- Diffuse
- Intestinal, Mix, others

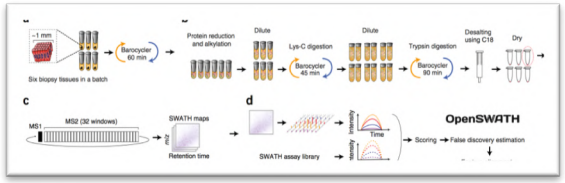
Ge, S., et al., Nature Communication, 2018. 9(1): p. 1012.
Mun, D.G., et al., Cancer Cell, 2019. 35(1): p. 111-124 e10.

Overview of our project

北京大学肿瘤医院
BEIJING CANCER HOSPITAL

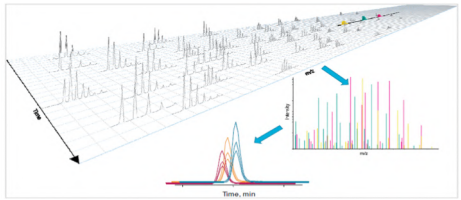


PCT : a method for clinical sample preparation



Tiannan Guo,2015

SWATH: Fast, accurate and reproducible DIA method

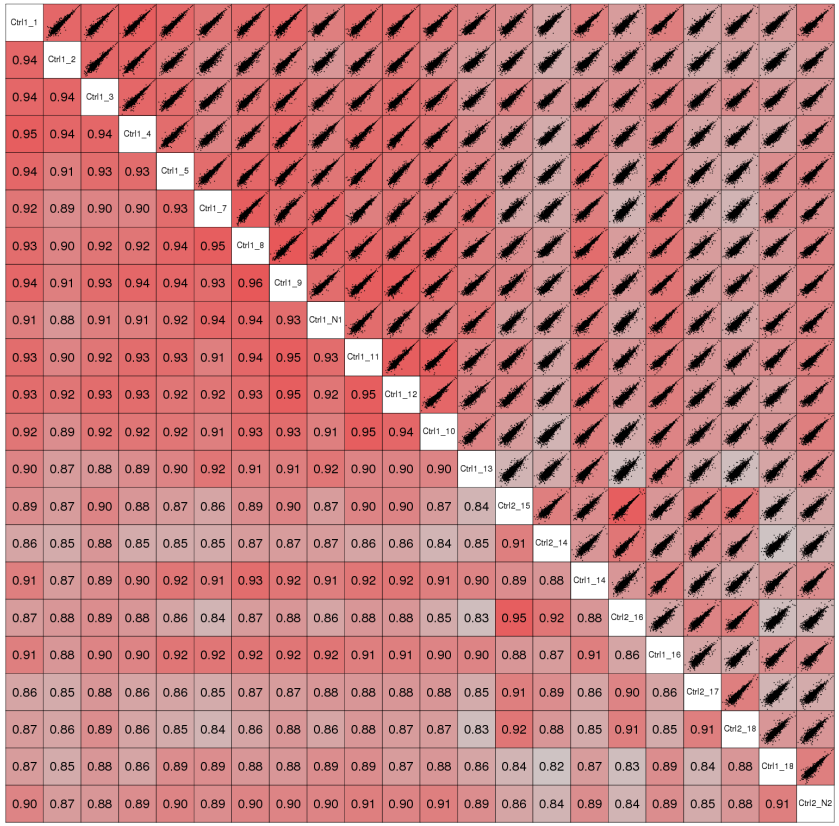


Rost, Hannes L, 2014

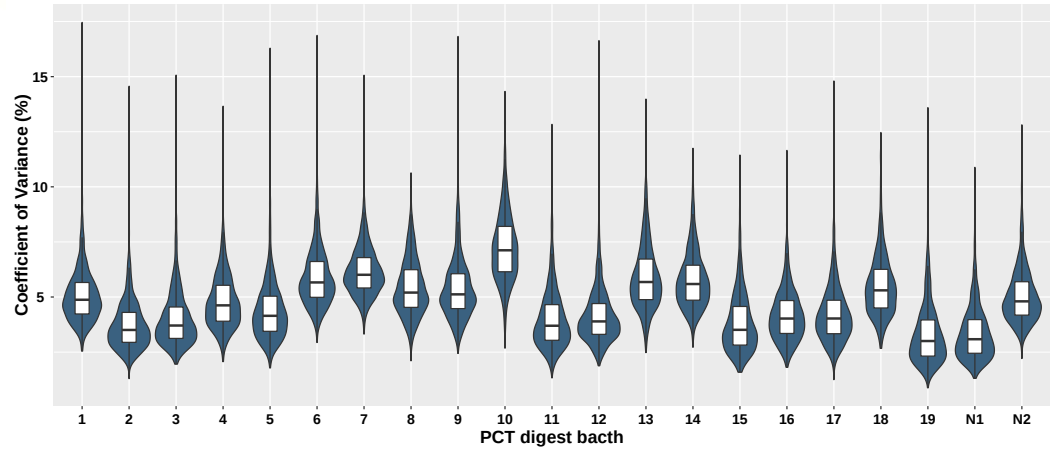
OpenSWATH

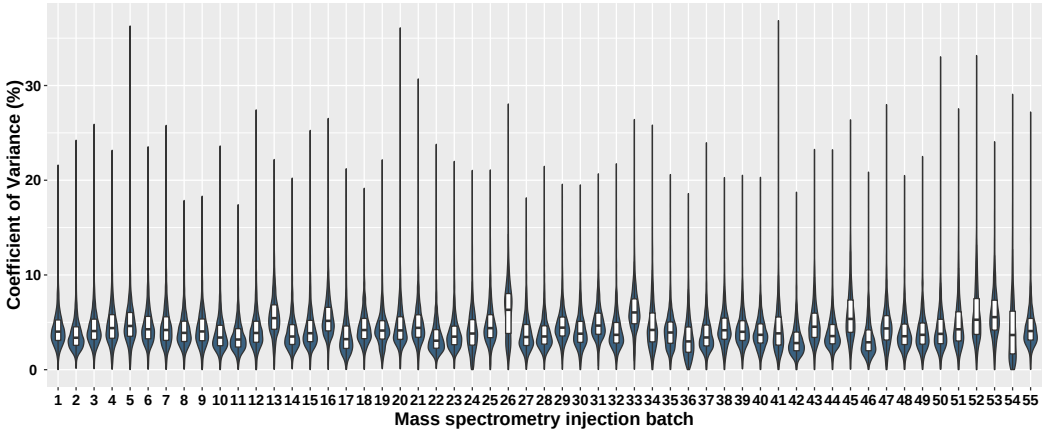
Unpublished data

Proteomics data quality



Correlation PCT Controls samples
Median correlation 0.9;
Range of correlation:0.82-0.96





Unpublished data

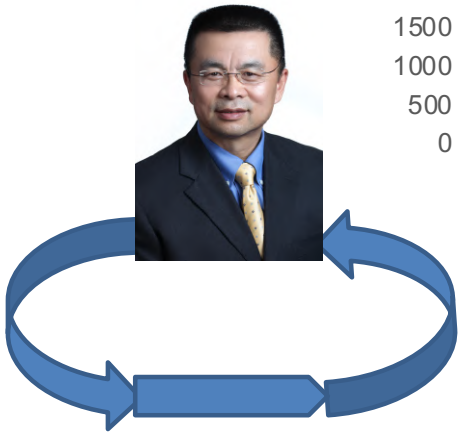
Multi-disciplinary International collaboration

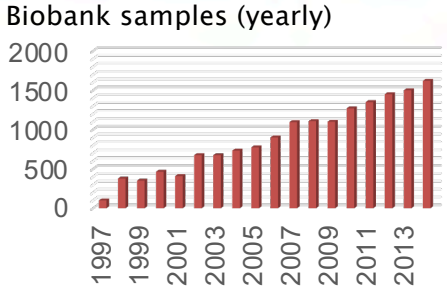
北京大学肿瘤医院
BEIJING CANCER HOSPITAL

Clinical Leader

Jiafu Ji M.D.

- Director of GI surgical center & President of Peking University Cancer Hospital
- President of International Gastric Cancer Association (**IGCA**)

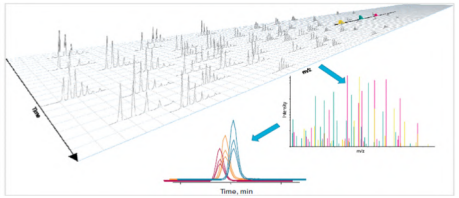




Proteomics Leader

Ruedi Aebersold Ph.D.

- ETH Zurich
- Inventor of PCT-SWATH



Genomics & Bioinfo Leader

Jianmin Wu Ph.D.

- Director of Center for Cancer Bioinformatics
- **ICGC-ARGO** Scientific Planning Committee member

Acknowledgements

北京大学肿瘤医院
BEIJING CANCER HOSPITAL

Center for Cancer Bioinformatics

Jianmin Wu, Ph.D.
Yang Du, Ph.D.
Sijia Cui, Ph.D.
Lihua Cao, Ph.D.
Man Wang, Ph.D.
Yang Yang, Ph.D.
Luxi Zhang, Ph.D.
Huan Yu
Xiaoqing Guan

Biobank

Lianhai Zhang, M.D.
Yin Hu

GI surgical center

Jiafu Ji, M.D.
Ziyu Li., M.D.
Shaode Bu, M.D.
Aiwen Wu, M.D.
Xiangqian Su, M.D.
Fei Shan, M.D.
XiangYu Gao, M.D.

Dept. of Pathology

Zhongwu Li, M.D.
Bin Dong, M.D.

University of Zurich, Switzerland

Ruedi Aebersold
Gillet Ludovic
Peng Xue

Westlake University

Tiannan Guo
Yi Zhu

International Cancer Genome Consortium

ARGO
International Cancer Genome Consortium
The ARGO Project

Contact: wujm@bjmu.edu.cn