Bioinformatics Institute
BII

BUILDING DISEASE DATA RESOURCES BY END-TO-END RESEARCH DATA INTEGRATION

Xing Yi Woo

Senior PI and Head of Research Data Integration

Biomedical Datahub Division

BII Conference 2023

Research Data Integration Group

Brandon Phua
Analysis pipelines
ISONET, RAPTOR
Database

Nicola Wong
Analysis pipelines
Downstream analysis leading to new biological findings

Chew Zhen Yuan
Spatial transcriptomics analysis workflow

Ayu
Molecular Tumor Board reporting

Lau Mai Chan
Spatial & Single-cell Omics Immunology

Jesslyn (IMCB)
Drug dosing analysis

Benjamin Chen (IMCB)
Metadata curation, Omics analysis

End-to-end research data integration to build disease data resources of biobanks

CREATING GROWTH, ENHANCING LIVES

Woo et al. BMC Medical Genomics (2019) 12:92
https://doi.org/10.1186/s12920-019-0551-2

BMC Medical Genomics

TECHNICAL ADVANCE Open Access

Genomic data analysis workflows for tumors from patient-derived xenografts (PDXs): challenges and guidelines

Xing Yi Woo[1†], Anuj Srivastava[1†], Joel H. Graber[3†], Vinod Yadav[1,3], Vishal Kumar Sarsani[2,4], Al Simons[2], Glen Beane[2], Stephen Grubb[2], Guruprasad Ananda[1], Rangjiao Liu[1,6], Grace Stafford[2], Jeffrey H. Chuang[1], Susan D. Airhart[2], R. Krishna Murthy Karuturi[1], Joshy George[1*] and Carol J. Bult[2*]

CANCER RESEARCH | TUMOR BIOLOGY AND IMMUNOLOGY

Systematic Establishment of Robustness and Standards in Patient-Derived Xenograft Experiments and Analysis

Yvonne A. Evrard[1], Anuj Srivastava[2], Jelena Randjelovic[3], The NCI PDXNet Consortium, James H. Doroshow[4], Dennis A. Dean II[3], Jeffrey S. Morris[5], and Jeffrey H. Chuang[2,6]

ARTICLES
https://doi.org/10.1038/s41588-020-00750-6
nature genetics

OPEN

Conservation of copy number profiles during engraftment and passaging of patient-derived cancer xenografts

Xing Yi Woo[1,6,14,15], Jessica Giordano[2,3,14], Anuj Srivastava[1], Zi-Ming Zhao[1], Michael W. Lloyd[4], Roebi de Bruijn[5], Yun-Suhk Suh[6], Rajesh Patidar[7], Li Chen[7], Sandra Scherer[8], Matthew H. Bailey[8,9], Chieh-Hsiang Yang[8], Emilio Cortes-Sanchez[8], Yuanxin Xi[10], Jing Wang[10], Jayamanna Wickramasinghe[11], Andrew V. Kossenkov[11], Vito W. Rebecca[12], Hua Sun[12], R. Jay Mashl[12], Sherri R. Davies[12], Ryan Jeon[12], Christian Frech[13], Jelena Randjelovic[13], Jacqueline Rosains[13], Francesco Galimi[2,3], Andrea Bertotti[2,3], Adam Lafferty[14], Alice C. O'Farrell[14], Elodie Modave[15,16], Diether Lambrechts[15,16], Petra ter Brugge[17], Violeta Serra[17], Elisabetta Marangoni[18], Rania El Botty[18], Hyunsoo Kim[1], Jong-Il Kim[19], Han-Kwang Yang[6], Charles Lee[1,9,20], Dennis A. Dean II[21], Brandi Davis-Dusenbery[12], Yvonne A. Evrard[22], James H. Doroshow[23], Alana L. Welm[8], Bryan E. Welm[8,22], Michael T. Lewis[23], Bingliang Fang[24], Jack A. Roth[24], Funda Meric-Bernstam[25], Meenhard Herlyn[21], Michael A. Davies[26], Li Ding[12], Shunqiang Li[12], Ramaswamy Govindan[12], Claudio Isella[2,3,15], Jeffrey A. Moscow[27,15], Livio Trusolino[2,3,15], Annette T. Byrne[14,15], Jos Jonkers[15,15], Carol J. Bult[6,15], Enzo Medico[2,3,15]✉, Jeffrey H. Chuang[1,15]✉, PDXNET Consortium* and EurOPDX Consortium*

CANCER RESEARCH | RESOURCE REPORT

A Genomically and Clinically Annotated Patient-Derived Xenograft Resource for Preclinical Research in Non-Small Cell Lung Cancer

Xing Yi Woo[1], Anuj Srivastava[1], Philip C. Mack[2], Joel H. Graber[3], Brian J. Sanderson[1], Michael W. Lloyd[3], Mandy Chen[2], Sergii Domanskyi[2], Regina Gandour-Edwards[4], Rebekah A. Tsai[2], James Keck[4], Mingshan Cheng[4], Margaret Bundy[4], Emily L. Jocoy[4], Jonathan W. Riess[2], William Holland[2], Stephen C. Grubb[3], James G. Peterson[3], Grace A. Stafford[3], Carolyn Paisie[1], Steven B. Neuhauser[3], R. Krishna Murthy Karuturi[1], Joshy George[1], Allen K. Simons[2], Margaret Chavaree[2,3], Clifford G. Tepper[2], Neal Goodwin[4], Susan D. Airhart[3], Primo N. Lara Jr[4], Thomas H. Openshaw[3], Edison T. Liu[5], David R. Gandara[2], and Carol J. Bult[3]

ARTICLES
https://doi.org/10.1038/s43018-022-00337-6
nature cancer

OPEN

A human breast cancer-derived xenograft and organoid platform for drug discovery and precision oncology

Katrin P. Guillen[1,2,13], Maihi Fujita[1,2,13], Andrew J. Butterfield[1,2,13], Sandra D. Scherer[1,2], Matthew H. Bailey[2,3], Zhengtao Chu[1,2], Yoko S. DeRose[1,2], Ling Zhao[1,2], Emilio Cortes-Sanchez[1,2], Chieh-Hsiang Yang[1,2], Jennifer Toner[1,2], Guoying Wang[1,2], Yi Qiao[3], Xiaomeng Huang[3], Jeffery A. Greenland[1,2], Jeffery M. Vahrenkamp[1,2], David H. Lum[1,2], Rachel E. Factor[2,4], Edward W. Nelson[2,5], Cindy B. Matsen[2,5], Jane M. Poretta[2,5], Regina Rosenthal[2,5], Anna C. Beck[2,6], Saundra S. Buys[2,6], Christos Vaklavas[2,6], John H. Ward[2,6], Randy L. Jensen[1,2,7], Kevin B. Jones[1,2,8], Zheqi Li[9], Steffi Oesterreich[9], Lacey E. Dobrolecki[10], Satya S. Pathi[1,2], Xing Yi Woo[11], Kristofer C. Berrett[1,2], Mark E. Wadsworth[1,2], Jeffrey H. Chuang[11,12], Michael T. Lewis[10], Gabor T. Marth[2,3], Jason Gertz[1,2], Katherine E. Varley[1,2], Bryan E. Welm[2,5,12] and Alana L. Welm[1,2,5,12]

nature COMMUNICATIONS

ARTICLE
https://doi.org/10.1038/s41467-021-25177-3 OPEN

Comprehensive characterization of 536 patient-derived xenograft models prioritizes candidates for targeted treatment

© 2022. Published by The Company of Biologists Ltd | Disease Models & Mechanisms (2022) 15, dmm049457. doi:10.1242/dmm.049457
The Company of Biologists

RESOURCE ARTICLE

Genetically diverse mouse platform to xenograft cancer cells

Jennifer K. Sargent[1,‡], Mark A. Warner[1,‡], Benjamin E. Low[1], William H. Schott[1], Todd Hoffert[1], David Coleman[1], Xing Yi Woo[2,*], Todd Sheridan[2,3], Sonia Erattupuzha[1], Philipp P. Henrich[1], Vivek M. Philip[1], Jeffrey H. Chuang[2], Michael V. Wiles[1] and Muneer G. Hasham[1,§]

NAR Cancer

Published online 22 April 2022

NAR Cancer, 2022, Vol. 4, No. 2 1
https://doi.org/10.1093/narcan/zcac014

PDXNet portal: patient-derived Xenograft model, data, workflow and tool discovery

Soner Koc[1,†], Michael W. Lloyd[2,†], Jeffrey W. Grover[1], Nan Xiao[1], Sara Seepo[1], Sai Lakshmi Subramanian[1], Manisha Ray[1], Christian Frech[3], John DiGiovanna[3], Phillip Webster[3], Steven Neuhauser[3], Anuj Srivastava[3], Xing Yi Woo[3], Brian J. Sanderson[3], Brian White[3], Paul Lott[4], Lacey E. Dobrolecki[5], Heidi Dowst[5], PDXNet Consortium, Yvonne A. Evrard[6], Tiffany A. Wallace[7], Jeffrey A. Moscow[8], James H. Doroshow[9], Nicholas Mitsiades[5], Salma Kaochar[5], Chong-xian Pan[4,10], Moon S. Chen[4], Luis Carvajal-Carmona[4], Alana L. Welm[11], Bryan E. Welm[11], Michael T. Lewis[5], Ramaswamy Govindan[12], Li Ding[12], Shunqiang Li[12], Meenhard Herlyn[13], Michael A. Davies[14], Jack Roth[14], Funda Meric-Bernstam[14], Peter N. Robinson[15], Carol J. Bult[12], Brandi Davis-Dusenbery[1], Dennis A. Dean, II[1,‡] and Jeffrey H. Chuang[2,*,‡]

bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

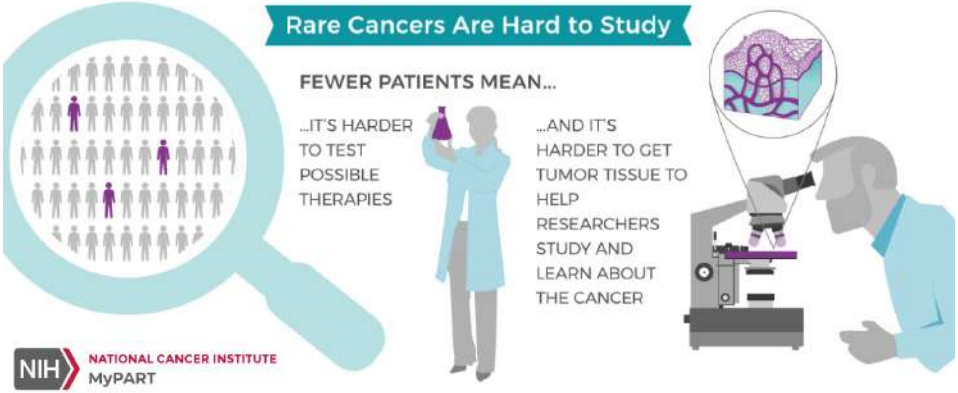
A pan-cancer PDX histology image repository with genomic and pathological annotations for deep learning analysis

Brian S White, Xing Yi Woo, Soner Koc, Todd Sheridan, Steven B Neuhauser, Shidan Wang, Yvonne A Evrard, John David Landua, R Jay Mashl, Sherri R Davies, Bingliang Fang, Maria Gabriela Raso, Kurt W Evans, Matthew H Bailey, Yeqing Chen, Min Xiao, Jill Rubinstein, Ali Foroughi pour, Lacey Elizabeth Dobrolecki, Maihi Fujita, Junya Fujimoto, Guanghua Xiao, Ryan C Fields, Jacqueline L Mudd, Xiaowei Xu, Melinda G Hollingshead, Shahanawaz Jiwani, PDXNet consortium, Brandi Davis-Dusenbery, Tiffany A Wallace, Jeffrey A Moscow, James H Doroshow, Nicholas Mitsiades, Salma Kaochar, Chong-xian Pan, Moon S Chen Jr, Luis G Carvajal-Carmona, Alana L Welm, Bryan E Welm, Ramaswamy Govindan, Shunqiang Li, Michael A Davies, Jack A Roth, Funda Meric-Bernstam, Yang Xie, Meenhard Herlyn, Li Ding, Michael T Lewis, Carol J Bult, Dennis A Dean II, Jeffrey H Chuang

doi: https://doi.org/10.1101/2022.10.26.512745

In Review: Nature Cancer Resource

FUTURE: FUnctional precision medicine and Translational resoUrce for RarE cancers



Unmet need: Lack effective therapies, disproportionately poor outcomes

TO IMPROVE OUTCOMES IN RARE CANCERS

We need...

- **Biomarkers** to predict patient *response* or *resistance* to treatments
- **Novel therapeutics** effective for patients who do not respond to existing options

We use...

- A **functional precision oncology** approach with **multimodal data analysis and integration**

National Cancer Centre Singapore SingHealth
Singapore General Hospital SingHealth
STCC Singapore Translational Cancer Consortium
NUS National University of Singapore | N.1
CSI SINGAPORE
EDDC Experimental Drug Development Centre
Institute of Molecular and Cell Biology IMCB
Singapore Immunology Network SIgN
Bioinformatics Institute BII

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Functional precision medicine in cancer

CellPress
OPEN ACCESS

Cancer Cell

Perspective

Functional precision oncology: Testing tumors with drugs to identify vulnerabilities and novel combinations

Anthony Letai,[1,2] Patrick Bhola,[2,3] and Alana L. Welm[4,*]
[1]Dana-Farber Cancer Institute, Boston, MA 02215, USA
[2]Harvard Medical School, Boston, MA 02215, USA
[3]Brigham and Women's Hospital, Boston, MA 02115, USA
[4]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT 84112, USA
*Correspondence: alana.welm@hci.utah.edu
https://doi.org/10.1016/j.ccell.2021.12.004

SUMMARY

Functional precision medicine is a strategy whereby live tumor cells from affected individuals are directly perturbed with drugs to provide immediately translatable, personalized information to guide therapy. The heterogeneity of human cancer has led to the realization that personalized approaches are needed to improve treatment outcomes. Precision oncology has traditionally used static features of the tumor to dictate which therapies should be used. Static features can include expression of key targets or genomic analysis of mutations to identify therapeutically targetable "drivers." Although a surprisingly small proportion of individuals derive clinical benefit from the static approach, functional precision medicine can provide additional information regarding tumor vulnerabilities. We discuss emerging technologies for functional precision medicine as well as limitations and challenges in using these assays in the clinical trials that will be necessary to determine whether functional precision medicine can improve outcomes and eventually become a standard tool in clinical oncology.

Patient derived model	Advantages	Disadvantages	Readouts to assess drug response
2D culture	• Rapid expansion • Low cost • High throughput • Amenable to rapid testing	• Prolonged ex vivo culture; assay dependent • Missing many microenvironment components • Non-physiologic culture conditions	Cell Viability
3D Organoids	• Mimics the 3D tumor environment • Moderate cost • Moderate throughput • Amenable to rapid testing; assay dependent	• Prolonged ex vivo culture; assay dependent • Missing some microenvironment components • Non-physiologic culture conditions	Gene/protein expression Tumor volume
Microfluidics & Engineered Microenvironments	• Engineered tumor microenvironment • Amenable to rapid testing; assay dependent	• Prolonged ex vivo culture; assay dependent • Missing some microenvironment components • Generally low throughput	Cell mass and morphology
Patient Derived Xenografts	• In vivo tumor environment • Incorporates drug pharmacokinetics • Clear toxicity readout	• Slow expansion • High cost • Low scalability • Tumor-host species differences • Lacking immune system	Mitochondrial priming
Human Patient	• Human microenvironment • Avoids model establishment	• Regulatory barriers • Biopsies required to rapidly assess response	Implantable microdevice

- Generate dynamic, functional data on tumor vulnerabilities
- Accompanied by data of genomic aberrancies e.g. altered signaling pathways

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"Rare" Cancer Functional Precision Oncology with Multimodal Data Analysis and Integration

Valerie Yang (NCCS, IMCB) Sample and clinical data collection, multi-omic profiling, cancer biology

Johnny Ong (NCCS) Tumor resection

Timothy Tay (SGH) Pathology

Tan Boon Toh (N.1, NUS) Models, drug screening

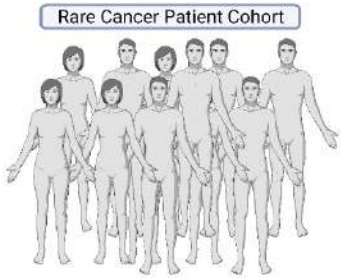
Yan Chuan (IMCB) Models, drug screening

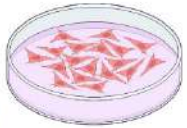
Qingfeng Chen (IMCB) Humanized mouse Models

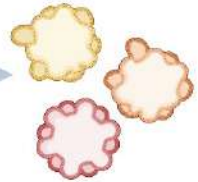
Edward Chow (CSI) Drug screening and optimization

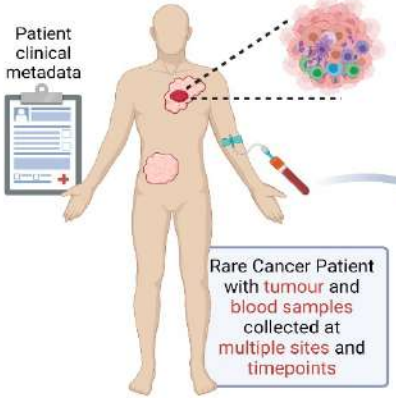
Zheng Ser (IMCB, Radek's group) Proteomics

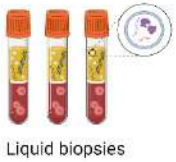
Xing Yi Woo (BII) Data coordination

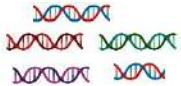


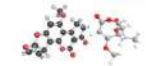


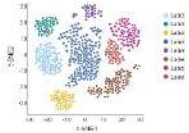


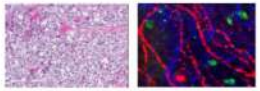


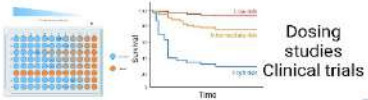








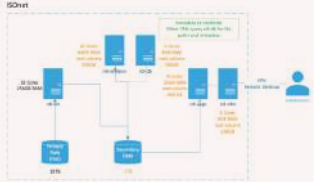




Systematic workflows
Integrative analysis
Structured databases
Data visualization

Mechanisms of sensitivity/resistance
Precision medicine
Patient stratification
Biomarker discovery

Powered by BioMed Dar



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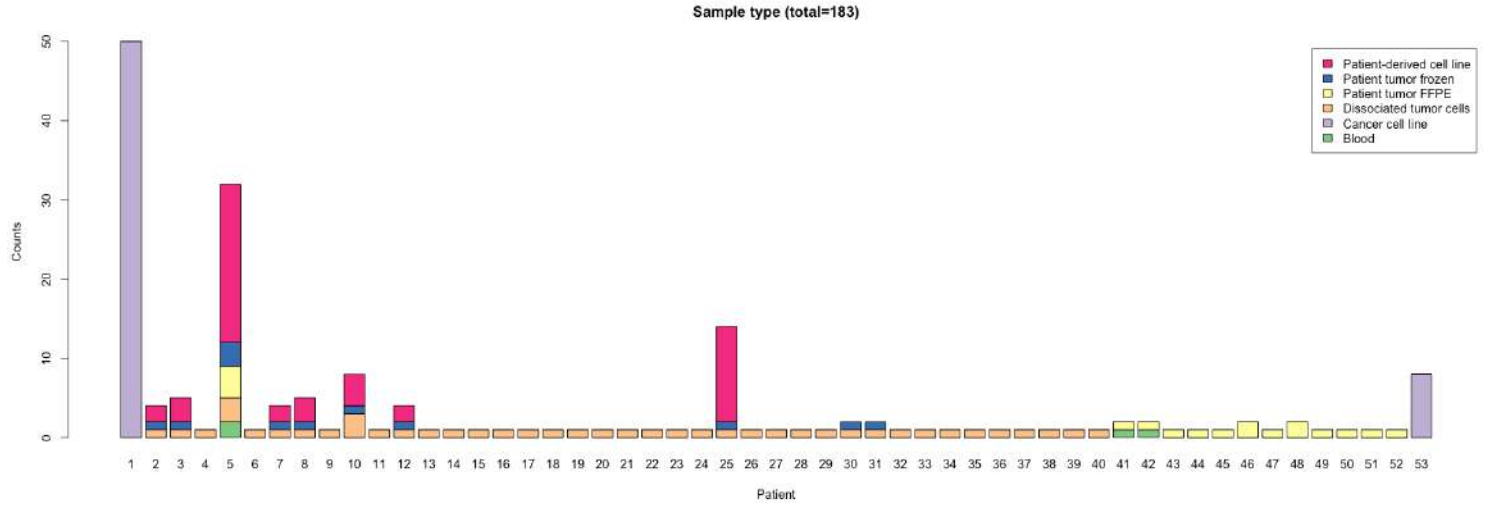
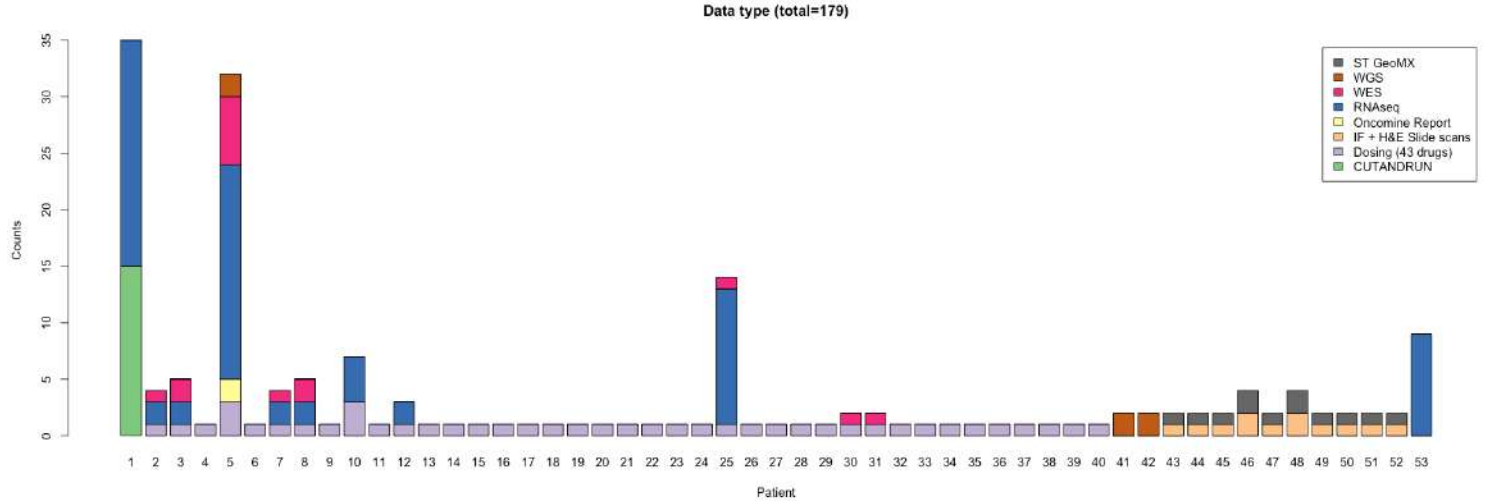
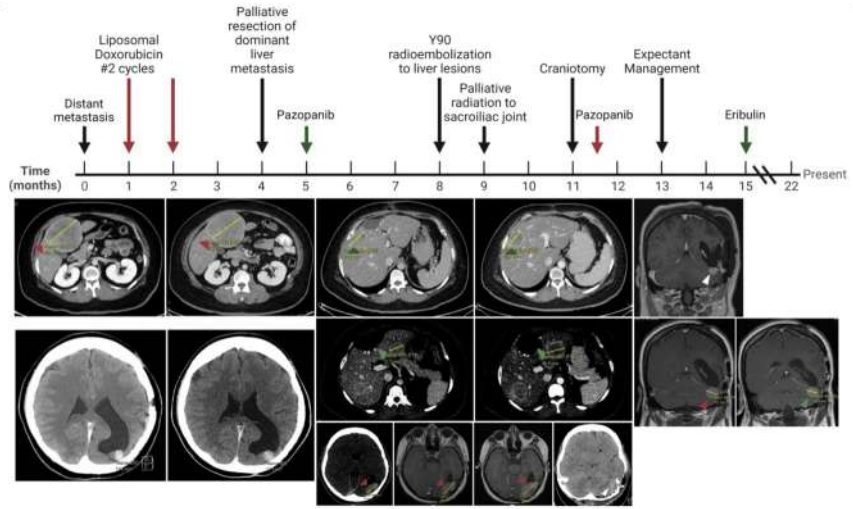
Growing data resource





FPM shows promise as a N-of-1 treatment approach (trial)



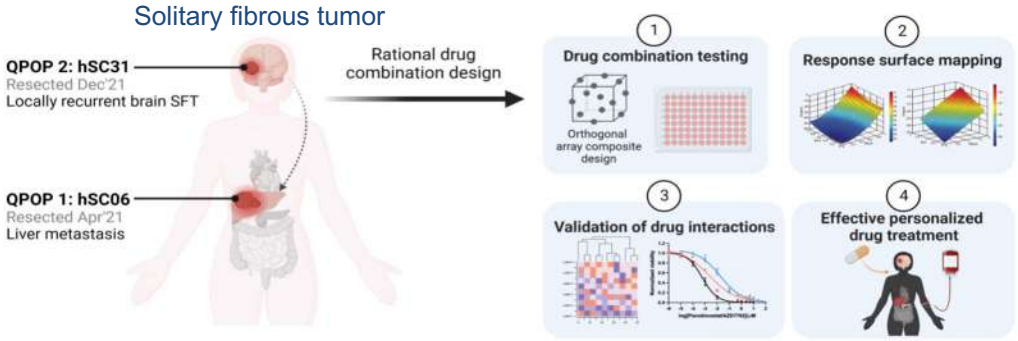
medRxiv — THE PREPRINT SERVER FOR HEALTH SCIENCES

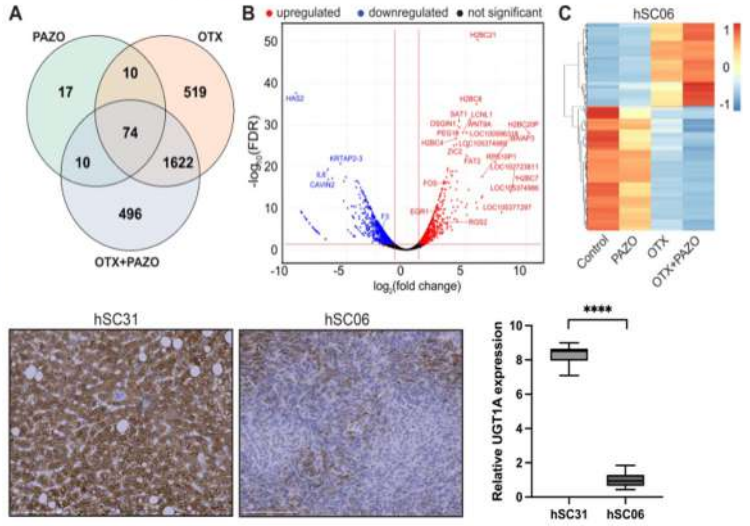
BMJ Yale

***Ex vivo* drug testing in an ultra-rare sarcoma reveals therapeutic vulnerability and resistance**

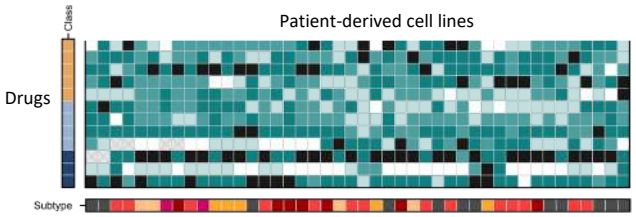
Sharon Pei Yi Chan, Baiwen Luo, Benjamin Jieming Chen, Andre Villanueva, Sam Xin Xiu, Benjamin Livingstone Farah, Nicholas Shannon, Chin-Ann Johnny Ong, Claramae Shulyn Chia, Ming-Hui Yong, Krishan Kumar, London Lucien Ooi, Timothy Kwang Yong Tay, Xing Yi Woo, Tan Boon Toh, Edward Kai-Hua Chow, Valerie Shiwen Yang

doi: https://doi.org/10.1101/2022.08.03.22278327

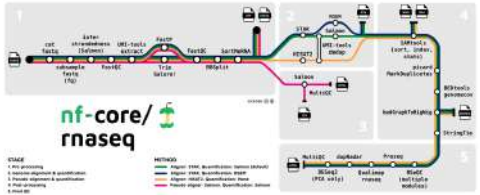


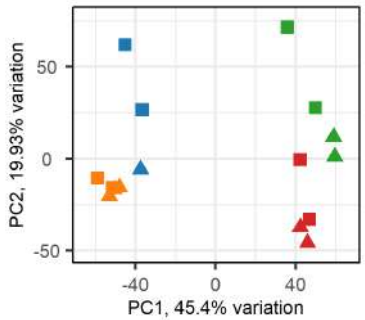


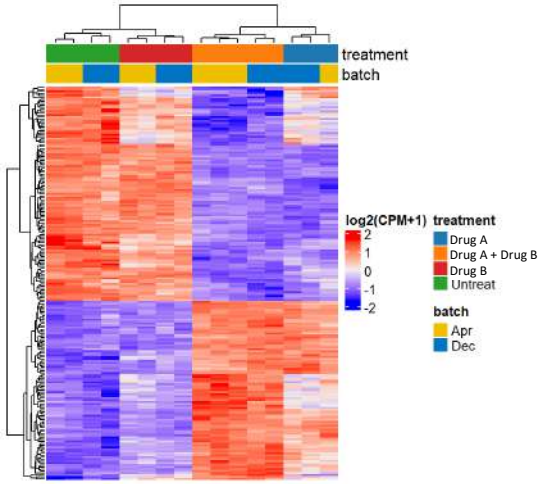
FPM by drug screening and biomarker discovery

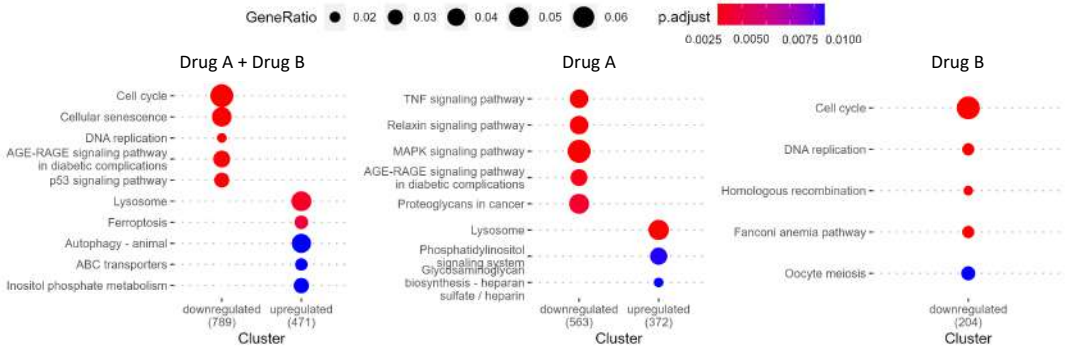


RNA-Seq









Future

1. Structural/functional predictions of cancer mutations


SEBASTIAN MAURER-STROH


CHANDRA VERMA


DANIEL TAN (NCCS)

2. Cancer Omics Platform


PATRICK TAN


TAM WAI LEONG

3. Brain-Body Initiative


HAN WEIPING


MICHAEL MEANEY

4. Non-alcoholic fatty liver disease


NG HUCK HUI

CREATING GROWTH, ENHANCING LIVES

CREATING GROWTH, ENHANCING LIVES

Bioinformatics Institute
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THANK YOU

www.a-star.edu.sg

woo_xing_yi@bii.a-star.edu.sg