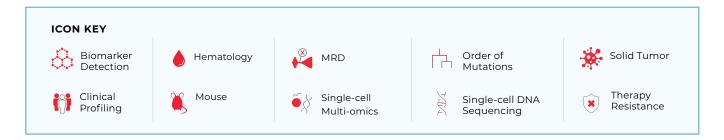
# **III** mission bio

# Publication List



#### 2022



#### Guess, T. et al., Blood Cancer Discovery

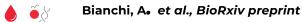
Distinct patterns of clonal evolution drive myelodysplastic syndrome progression to secondary acute myeloid leukemia

• Used DNA + protein multi-omics to characterize the clonal architecture and evolution in MDS patients who progress to sAML.

## 🤞 📩 🔹 Droskea, L. et al., BioRxiv preprint

High-throughput single-cell sequencing for retroviral reservoir characterization

Described a scDNA-seq method optimized for sequencing of proviral and host DNA for retroviral reservoir characterization.



scTAM-seq enables targeted high-confidence analysis of DNA methylation in single cells

 Developed scTAM-seq, a targeted bisulfite-free method for analyzing DNA methylation at single-CpG resolution across thousands of single cells.

### 🍯 🕂 Maslah, N. et al., Blood Advances

Single-cell analysis reveals selection of TP53-mutated clones after MDM2 inhibition

• Demonstrated that MDM2 treatment can directly favor the emergence of TP53-mutated subclones in chronic myeloproliferative neoplasms (MPN).







## Meyers, S. et al., HemaSphere

Monitoring of Leukemia Clones in B-cell Acute Lymphoblastic Leukemia at Diagnosis and During Treatment by Single-cell DNA Amplicon Sequencing

· Characterized the mutational heterogeneity and evolution in B-ALL, both at diagnosis and during treatment.

## 🔆 🏹 📩 Zhang, H. et al., BioRxiv preprint

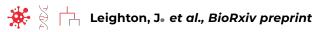
Application of high-throughput, high-depth, targeted single-nucleus DNA sequencing in pancreatic cancer

- · Optimized a highly automated nuclei extraction workflow that achieved fast and reliable
  - targeted single-nucleus DNA library preps from pancreatic adenocarcinoma (PDAC) patients

## 🖗 📩 🟠 Snellings, D.A. et al., Nature Cardiovascular Research

Developmental Venous Anomalies are a Genetic Primer for Cerebral Cavernous Malformations

 Adapted sc-DNA sequencing to evaluate the relationship between developmental venous anomalies (DVAs) and cerebral cavernous malformations (CCMs)



Reconstructing mutational lineages in breast cancer by multi-patient targeted single cell DNA sequencing

· Developed a Multi-Patient-Targeted (MPT) scDNA-sequencing method to study tumor evolution in breast cancer

## 🦉 📩 Kim, T. et al., British Society for Hematology

Single cell proteogenomic sequencing identifies a relapse-fated AML subclone carrying FLT3-ITD with CN-LOH at chr13g

· Used DNA + protein multi-omics to detect a relapse-fated subclone at the time of initial diagnosis that was enriched with homozygous 21 bp FLT3-ITDs.

#### $\mathbf{x}$ Blombery, P E. et al., Blood

Clonal hematopoiesis, myeloid disorders and BAX-mutated myelopoiesis in patients receiving venetoclax for CLL

· Sc-DNA sequencing revealed patterns of co-occuring BAX mutations in the myeloid compartments of CLL patients receiving venetoclax therapy





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#### 🔍 💌 🛛 Wang, E🛛 et al., The New England Journal of Medicine

Mechanisms of Resistance to Noncovalent Bruton's Tyrosine Kinase Inhibitors. The New England Journal of Medicine

Identified clonal architecture of resistance mutations to a new class of non-covalent BTK inhibitors in CLL patients

#### X Zhang, Q. et al., Signal Transduction and Target Therapy

Activation of RAS/MAPK pathway confers MCL-1 mediated acquired resistance to BCL-2 inhibitor venetoclax in acute myeloid leukemia

Identified the activation of RAS/MAPK pathway, leading to increased stability and higher
levels of MCL-1 protein, as a major acquired mechanism of VEN resistance in AML.

## Rodriguez, S. et al., Science Advances

Preneoplastic somatic mutations including MYD88 L265P in lymphoplasmacytic lymphoma

 DNA + protein multi-omics demonstrated that mutation in a gene relevant to B cell function, such as MYD88, represents a preneoplastic event that requires additional genetic alterations to drive lymphomagenesis

#### 2021

#### Thompson E.R. et al., Blood Advances

Single-cell sequencing demonstrates complex resistance landscape in CLL and MCL treated with BTK and BCL2 inhibitors

 Identified clonal architecture of acquired genomic resistance to BTK and BCL2 inhibitors in CLL and MCL patients.



Diverse alterations associated with resistance to KRAS(G12C) inhibition

• Revealed a heterogeneous pattern of resistance involving many genes and multiple subclonal events emerging during KRAS (G12C) inhibitor treatment for lung and colorectal cancer.



#### Sharma R. et al., *Blood*

Gain-of-function mutations in RPAI cause a syndrome with short telomeres and somatic genetic rescue

 Single-cell DNA+protein multi-omics revealed somatic genetic rescue events that evolved independently in HSPCs, myeloid cells, and B-cells in patients with telomere disorders.



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#### 2021 cont.



#### Sahoo S.S. et al., Nature Medicine

Clinical evolution, genetic landscape, and trajectories of clonal hematopoiesis in SAMD9/SAMD9L syndromes

• Uncovered diversity of somatic genetic rescue events in pediatric instances of SAMD9/9L syndromes, some of which serve as "natural gene therapy."

#### 🖲 🏹 Dillon L.W. et al., Blood Cancer Discovery

Personalized single-cell proteogenomics to distinguish acute myeloid leukemia from nonmalignant clonal hematopoiesis

• Distinguished malignant variants of AML from age-related clonal hematopoiesis by resolving immunophenotypic identity of clonal architecture.



#### Marin-Bejar, O. et al., Cancer Cell

Evolutionary predictability of genetic versus nongenetic resistance to anticancer drugs in melanoma

· An analysis of genetic and nongenetic mechanisms of therapy resistance in melanoma.



#### Thijssen, R. et al., *Blood*

Intact TP-53 function is essential for sustaining durable responses to BH3-mimetic drugs in leukemias

Revealed the effect of TP-53 mutation status on treatment of AML with the BH3-mimetic drugs.



#### Wang, F. et al., Nature Communications

Leukemia stemness and co-occurring mutations drive resistance to IDH inhibitors in acute myeloid leukemia

 Investigated clones that enabled relapse in AML patients who received IDH inhibitor treatment.



#### Ren, A. et al., Nature

PIK3CA and CCM mutations fuel cavernomas through a cancer-like mechanism

 Single-nuclei sequencing revealed patters of co-mutation that promote cerebral cavernous malformations (CCMs).



#### Lim, K.H. et al., Blood Advances

Clonal evolution and heterogeneity in advanced systemic mastocytosis revealed by single-cell DNA sequencing

• Investigation of resistance to the multikinase inhibitor, midostaurin, in patients with advanced systemic mastocytosis (advSM).





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#### Demaree, B. et al., Nature Communications

Joint profiling of DNA and proteins in single cells to dissect genotype-phenotype associations in leukemia

 Genotype & immunophenotype "decoupling" in leukemias samples was revealed using singlecell multi-omics.



#### Peretz, C.A. et al., Blood Advances

Single cell DNA sequencing reveals complex mechanisms of resistance to quizartinib

Investigated mechanisms of resistance to quizartinib in patients with FLT3-ITD mutated AML.



### 📕 🛛 Ilacobucci, I. et al., *Blood*

Modeling and targeting of erythroleukemia by hematopoietic genome editing

• Used scDNA-seq analyze CRISPR-edited cells in preclinical models of acute erythroid leukemia (AEL).

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Distinct genetic pathways define pre-malignant versus compensatory clonal hematopoiesis in Shwachman-Diamond syndrome

• Zygosity and CN-LOH are reliably measured with high sensitivity (0.1%) and predict progression to leukemia in patients with Shwachman-Diamond syndrome.

## 💧 🞁 💾 Alberti-Servera, L. et al., Blood

Single-cell DNA amplicon sequencing reveals clonal heterogeneity and evolution in T-cell acute lymphoblastic leukemia

• First study to assess the clonality and order of mutation acquisition of T-cell acute lymphoblastic leukemia (T-ALL) patient samples.



#### Patel, B.A. et al., Haematologica

Detectable mutations precede late myeloid neoplasmia in aplastic anemia

• Identified evolution of mutations in a rare case where an severe aplastic anemia (SAA) patient who received immunosuppressive therapy developed MDS/AML with normal cytogenetics.



#### Thompson E.R. et al., Haematologica

Clonal independence of *JAK2* and *CALR* or *MPL* mutations in comutated myeloproliferative neoplasms demonstrated by single cell DNA sequencing

• First publication in T-cell acute lymphoblastic leukemia (T-ALL) that highlights SNVs/indels and MRD detection.





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## 🌔 🍯 🏹 📩 Miles, L.A. et al., Nature

Single-cell mutation analysis of clonal evolution in myeloid malignancies

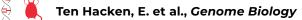
 Used DNA + protein multi-omics to assess clonal architecture and evolution of AML, MPN, and clonal hematopoiesis.



## 🖕 🍝 🕂 Morita, K. et al., Nature Communications

Clonal evolution of acute myeloid leukemia revealed by high-throughput single-cell genomics

· Extensive study investigating genotype and immunophenotype associated with clonal evolution in AML.



High throughput single-cell detection of multiplex CRISPR-edited gene modifications

· Analyzed single and multiplexed CRISPR edits in individual cells in models of chronic lymphocytic leukemia (CLL).

#### Ö Xiao, W. et al., Blood Advances

A JAK2/IDH1-mutant MPN clone unmasked by ivosidenib in an AML patient without antecedent MPN

· Clonal architecture of a relapsed AML patient, in which treatment with an IDH1 inhibitor promoted outgrowth of a minor myeloid neoplasm (MPN) clone.



#### Taylor, J. et al., Blood

Single-cell genomics reveals the genetic and molecular bases for escape from mutational epistasis in myeloid neoplasms

 Studied a rare phenomenon in biology where 2 splicing mutations co-occur in the patient sample.



#### Maia, C. et al., Blood

Biological and clinical significance of dysplastic hematopoiesis in patients with newly-diagnosed multiple myeloma

 Identified biomarkers from multiple myeloma samples that develop into MDS using multidimensional flow cytometry and single-cell DNA-seq.



#### 🍐 🕂 💌 Choe, S. et al., Blood Advances

Molecular mechanisms mediating relapse following ivosidenib monotherapy in IDH1-mutant relapsed or refractory AML

 Biopharma study that showed molecular resistance mechanisms in 174 patients following ivosidenib monotherapy for R/R AML.







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## 🕨 🔆 💌 DiNardo, C.D. et al., *Blood*

Molecular patterns of response and treatment failure after frontline venetoclax combinations in older patients with AML

• Molecular basis for treatment resistance or durable remission in older patients with AML given venetoclax combination therapy.

#### 🛛 🗸 💌 Ediriwickrema, A. et al., Blood Advances

Single-cell mutational profiling enhances the clinical evaluation of AML MRD

MRD detection identified clones at remission that expanded into the dominant clone at relapse in patients with AML.

#### 2019



#### Xu, L. et al., Scientific Reports

Clonal evolution and changes in two AML patients detected with a novel single-cell DNA sequencing platform

Clonal remodeling in patients with AML after bone marrow transplant revealed donor chimerism and unique clones.

#### 💌 🎽 Gao, Y. et al., Cancer Discovery

V211D mutation in MEK1 causes resistance to MEK inhibitors in colon cancer

• Treatment resistance mechanism revealed in colon cancer PDX model after treatment with MEK inhibitor binimetinib and EGFR antibody panitumumab.

#### 💌 🙌 McMahon, C. et al., Cancer Discovery

Clonal selection with Ras pathway activation mediates secondary clinical resistance to selective FLT3 inhibition in acute myeloid leukemia

• Treatment resistance mechanism revealed in AML with co-occurring FLT3 and RAS mutations after treatment with the FLT3-inhibitor gilteritin in patients with AML.

#### 2018

#### Pellegrino, M. et al., Genome Research

High-throughput single-cell DNA sequencing of acute myeloid leukemia tumors with droplet microfluidics

• First publication that showcased single-cell DNA sequencing of thousands of cells using droplets in longitudinal AML sample.



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