China’s top 10 hematologic advances in 2020

Xiaochen Wang
Managing Editor, Blood Science, State Key Laboratory of Experimental Hematology, National Clinical Research Center for Blood Diseases, Institute of Hematology & Blood Diseases Hospital, Chinese Academy of Medical Sciences, 288 Nanjing Road, Tianjin 300020, China

From the research completed in China and published between January 1 and December 31, 2020, 25 candidates were selected through comprehensive retrieval by information agencies and recommendation by hematology experts. The final “China’s top 10 hematologic advances in 2020” were ranked by online voting from national academicians, the editorial board of the Chinese Journal of Hematology, and committee members from the Hematology Branch of Chinese Medical Association, Chinese Association of Blood Sciences, and Experimental Hematology Branch of Chinese Association of Pathophysiology. The result was announced on January 30, 2021, at the first China Blood Development Conference.

1. EARLY FATE CHOICES AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

The rapid advancement of single-cell RNA technology has created a powerful tool and an unprecedented opportunity to uncover the previously inaccessible “black box” of kinetics and fate choices of transplanted hematopoietic stem cells (HSCs) at an early stage. The research from Tao Cheng’s team provided a transcriptional map of human blood cells at single-cell resolution, providing a comprehensive reference for the study of physiological and pathological hematopoiesis.

Original research:
Nat Cell Biol. 2020 Jun;22 (6):630-639. https://www.nature.com/articles/s41566-020-0512-1
Natl Sci Rev. 2020 Oct 8;8(10):1093-1097. https://academic.oup.com/nsr/advance-article/doi/10.1093/nsr/nwaa180/5896476

2. EARLY ORIGIN OF HEMATOPOIETIC STEM PROGENITOR CELLS

At mid-gestation, the first HSCs with long-term repopulating potential in mammalian embryos differentiate from hemogenic endothelial cells (HECs), which are widely believed to be originated from arterial endothelial cells (ECs). Bing Liu’s team developed a research paradigm for defining putative HSCs based on transcriptome, immunophenotype, and function (TIF) at the single-cell level, which accurately captured HSC-competent HECs and human embryonic myeloid progenitor cells, revealed the origin of endothelial and hematopoietic cells, and characterized multiple origins of human macrophage cells as well as key molecular events in the spatiotemporal dynamics of early macrophage development during human embryogenesis.

Original research:
Nature 2020 Jun;582 (7813):571-576. https://www.nature.com/articles/s41586-020-2316-7
Cell Res. 2020 May;30(5):376-392. https://www.nature.com/articles/s41422-020-0300-2

3. DECODING HUMAN MEGAKARYOCYTE DEVELOPMENT

Despite our growing understanding of embryonic immune development, due to the extreme rarity of megakaryocytes (MKs) in early development and the limited accessibility of human embryonic and fetal tissues, MKs development remain relatively understudied. Again, using the cutting-edge technology, Jiaxi Zhou’s team investigated the molecular characteristics and heterogeneity of MKs in early human embryos by performing single-cell transcriptomics analysis, thereby revealing MK heterogeneity, discovering early megakaryopoietic trajectories, and identifying THBS1 as a marker for MK-biased ECs.

Original research:
Cell Stem Cell. 2021 Mar 4;28(3):535-549.e8. https://www.sciencedirect.com/science/article/pii/S1934590920305440?via%3Dihub

4. GENOMIC AND TRANSCRIPTOMIC CHARACTERIZATION OF NATURAL KILLER/T-CELL LYMPHOMA

Natural killer/T-cell lymphoma (NKTL) is a rare and aggressive type of non-Hodgkin lymphoma that is strongly associated with Epstein-Barr virus infection. Wei-Li Zhao’s team proposed an updated molecular subtyping scheme based on integrated analysis of the genomic and transcriptomic features of NKTL from patient biopsies, providing insights into the pathogenesis and therapeutic targeting of the disease.

Original research:
Cancer Cell 2020 Mar 16;37(3):403-419.e6. https://www.sciencedirect.com/science/article/pii/S1535610820300945?via%3Dihub
5. NOVEL THERAPEUTIC STRATEGY TARGETING ONCOGENIC MYC IN LEUKEMIA

MYC (also known as c-MYC) is broadly deregulated in human cancers such as T-cell acute lymphoblastic leukemia (T-ALL). Hudan Liu’s team described how AURKB-mediated phosphorylation stabilizes MYC to prevent its degradation by FBXW7 in T-ALL and demonstrated that MYC induces AURKB transcription to support leukemogenesis. These findings provided a rationale for the therapeutic targeting of oncogetic MYC via AURKB inhibition.

Original research:
Cancer Cell 2020 Feb 10;37(2):200-215.e5. https://www.sciencedirect.com/science/article/pii/S1535610820300404?via%3Dihub

6. MECHANISM OF CHROMATIN ALTERATIONS REGULATING THE FUNCTION OF LEUKEMIA STEM CELLS

N6-methyladenosine (m6A) is a common modification of mammalian mRNAs that plays important roles in a variety of cellular processes. Haojian Zhang’s team discovered that m6A demethylase ALKBH5 is specifically required for maintaining the function of acute myeloid leukemia (AML) stem cells but not normal HSCs and revealed KDM4C (a histone demethylase that is crucial for maintaining homeostasis in normal HSCs) as a novel therapeutic target. These findings laid the groundwork for targeting ALKBH5 for AML therapy.

Original research:
Cell Stem Cell 2020 Jul 2;27(1):81-97.e8. https://www.sciencedirect.com/science/article/pii/S1934590920301405?via%3Dihub

7. COMPLEMENT SIGNALS DETERMINE OPPOSITE EFFECTS OF B-CELLS IN CHEMOTHERAPY-INDUCED IMMUNITY

Understanding the molecular mechanisms that govern B-cell diversity is critical for targeting B-cells as an anti-cancer treatment. Through the single-cell dissection of B-cell heterogeneity in longitudinal samples of patients with breast cancer before and after neoadjuvant chemotherapy, Shicheng Su’s team discovered an ICOSL+B-cell subset after chemotherapy. In response to chemotherapy-induced immunomodulatory cell death and complement signaling response, an anti-tumoral B-cell subset emerges in the tumor microenvironment, which has implications for developing novel anti-cancer therapies.

Original research:
Cell 2020 Mar 19;180(6):1081-1097.e24. https://www.sciencedirect.com/science/article/pii/S0092867420315987?via%3Dihub

8. SORAFENIB MAINTENANCE IN PATIENTS WITH FLT3-ITD ACUTE MYELOID LEUKEMIA UNDERGOING ALLOGENIC HSC TRANSPLANTATION

FLT3 internal tandem duplication (FLT3-ITD) mutations occur in approximately 25% of adult AMLs. Even allogeneic HSC transplantation could improve the survival of AML patients, relapse of those with FLT3-ITD mutations remains relatively high. In patients with FLT3-ITD AML undergoing allogeneic HSC transplantation, Qifa Liu’s team demonstrated that sorafenib maintenance post-transplantation could reduce relapse and is well tolerated. This strategy could be a treatment option for patients with FLT3-ITD AML.

Original research:
Lancet Oncology 2020 Sep;21(9):1201-1212. https://www.sciencedirect.com/science/article/pii/S1470204520304551?via%3Dihub

9. RISK FACTORS IN THE CLASSIFICATION AND PROGNOSIS EVALUATION OF COVID-19

During the global pandemic, Yu Hu’s team aimed to investigate the hematological characteristics and associated risk factors in COVID-19 patients. They proposed a scoring system for sepsis-induced coagulopathy that could be used for early assessment and management of patients with critical diseases. Furthermore, they discovered that the prevalence of deep vein thrombosis (DVT) is high and is associated with poor outcomes in hospitalized patients with COVID-19, implying that COVID-19 is likely an additional risk factor for DVT in hospitalized patients.

Original research:
Circulation 2020 Jul 14;142(2):114-128. https://www.aha.org/authors/journals.org/doi/10.1161/CIRCULATIONAHA.120.046702?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
Lancet Haematology 2020 Sep;7(9):e671-e678. https://www.sciencedirect.com/science/article/pii/S2352302620302179?via%3Dihub

10. PREVENTION AND TREATMENT OF HEPATITIS B VIRUS REACTIVATION AFTER CAR T-CELL THERAPY

Several research teams (Jianfeng Zhou, Lugui Qiu, Kailin Xu, Wenbin Qian, etc.) discovered that hepatitis B virus (HBV) reactivation is at high risk in patients with HBV infection when receiving chimeric antigen receptor-engineered (CAR) T-cell therapy, and treatment with nucleoside analogs is essential to prevent HBV reactivation in these patients. These studies provided a solid foundation for developing guidelines for CAR T-cell therapy-related adverse reactions.

Original research:
Blood 2020 Jul 23;136(4):516-519. https://ashpublications.org/blood/article-abstract/136/4/516/454385/Entecavir-prophy laxis-for-hepatitis-B-virus?redirectedFrom=fulltext
Leukemia 2020 Oct;34(10):2704-2707. https://www.nature.com/articles/s41375-020-0936-4
Leukemia. 2020 Nov;34(11):3055-3059. https://www.nature.com/articles/s41375-020-0913-y
Br J Haematol 2020 Oct;191(1):126-129. https://onlinelibrary.wiley.com/doi/10.1111/bjh.16951