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Coming Back to In-Person Hematology: ASH 2021, A Re-Cap

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With relaxing COVID-19 restrictions toward the end of 2021, the American Society of Hematology (ASH) made a decision to offer a hybrid online/in-person format for the first time in Atlanta, USA. With this decision, ASH 2021 became a reference point on how to organize a hybrid meeting, and how to bring the hematology community together by engaging attendees both in-person and remotely.

ISEH members had the chance to attend the best experimental hematology sessions both online and in-person, a number of which focused on the biology of clonal hematopoiesis and new molecular mechanisms driving malignant transformation, and are highlighted below. We also interviewed our ISEH member Dr. Alba Rodriguez-Meira, who presented her work through one of the Plenary Sessions at ASH 2021.

A Few Highlights from ASH21 Sessions

Taking advantage of state-of-the-art whole-genome sequencing technologies, Dr. Emily Mitchell from the Campbell Lab (Sanger Institute, Cambridge; Abstract 598) detailed their group's study of greater than 3500 genomes of single clone derivatives of hematopoietic stem and progenitor cells from 10 hematologically normal subjects aged 0 to 81 years of age and determined that clonal diversity universally decreased with age, a process that is underpinned by pervasive positive selection on genetic drivers that are far greater in

number than has been understood to date.

Complementing this approach, Dr. Caroline Watson from the Blundell Lab (University of Cambridge; Abstract 599) presented their group's longitudinal study in which serial peripheral blood samples were retrospectively sequenced for myeloid-associated driver mutations and chromosomal abnormalities in patients prior to and up to the point of being diagnosed with acute myeloid leukemia (AML). By inferring the fitness advantages of distinct genetic subclones, they traced back pre-leukemic mutations (such as those found in clonal hematopoiesis of indeterminate potential (CHIP)) to approximately 20 years before a second genetic hit was acquired, and 50 years before the development of AML. Importantly, the fitness advantage of early clones influenced the onset of AML development, providing support for the importance and role of risk stratification and early intervention with such surveillance strategies.

Novel methodologies to assess the fitness effects of CHIP-related mutations were also presented. For example, Dr. Kristina Kirschner (CRUK Beatson Institute, University of Glasgow; pre-meeting workshop) presented a new computational method to extract fitness effects from longitudinal sequencing data using Bayesian inference while considering individual mutational context and co-occurrence of mutations, and thus quantify the growth potential of variants within each individual. Their groups' work showed that gene-specific fitness differences can outweigh inter-individual variation and supports a basis for personalized clinical management. Jk Gopakumar from the Jaiswal Lab (Stanford University; Abstract 597) introduced PACER, a new method to infer clonal expansion rates from serial single timepoint bulk whole-genome sequencing data. Their group applied a genome-wide association study to identify germline variants that correlated with PACER-estimated clonal expansion rate, and found that a common single nucleotide polymorphism in the promoter of TCL1A protected against TET2-mediated clonal expansion.

Several groups also focused on the underlying mechanisms of CHIP-mediated clonal expansions with elegant functional studies. For example, probing the methylation-independent effect of DNMT3A mutations using catalytically inactive mutants (presented by Won Kyun Koh from the Challen Lab, Washington University School of Medicine, Abstract 24), mechanisms of inflammation-related clonal advantage of DNMT3A mutations driven by p53 stabilization (presented by Dr. Christine Zhang, Challen Lab, Abstract 600) and fatty bone marrow (presented by Naama Zioni, Shlush Lab at the Weizmann Institute, Abstract 596).

Among studies focused on reconciling molecular mechanisms driving disease included one from Dr. Andreea Reilly, from the Doulatov Lab (University of Washington; Abstract 502), whose group showed how loss of LMNB1, a gene commonly deleted by 5q-MDS, leads to loss of self-renewal, myeloid bias, changes in the 3D genome organization responsible for aberrant lineage specification and characteristic morphological findings among neutrophils in this MDS subtype.

Many of the main scientific sessions at the Presidential Symposium focused on the biology of TP53, the

most recurrently mutated oncogene in cancer and associated with extremely poor prognosis in hematological malignancies. Dr. Carol Prives discussed fundamental biological mechanisms of p53-driven tumorigenesis and Dr. Guillermina Lozano and Dr. Matthew Davids, the latest therapeutic approaches related to p53-mutant inbition. Dr. Alba Rodriguez-Meira from the Mead Lab (University of Oxford, Abstract 3) identified inflammatory stimuli that drive disease transformation in the context of TP53-mutated myeloproliferative neoplasms.[RMA1] We had a chance to interview her during the conference, and you can read her experience below.

Interview with Dr. Alba Rodriguez Meira at ASH21

How did you enjoy ASH this year?

It was an amazing experience to finally see colleagues after two years in a much more interactive way. I just moved to the US so I can meet US colleagues in person now and extend my network.

What was the ASH highlight for you?

Being in the backstage room in the plenary session before my talk seeing all the preparations that go into a Plenary Session. I also got a lot of energy from interactions with colleagues and feeling alive in the scientific community.

How did you manage to have your abstract selected for the plenary session?

It was just the right combination of innovative technology and interesting biology that was timely with current trends in hematology research looking into TP53 mutated neoplasms.

How was your experience giving this talk?

Honestly, it was very overwhelming; the music upon entry was very intimidating but I thought it was such a good opportunity. I actually enjoyed the session very much at the end.

What helped you to deliver a good talk?

Thanks for saying it was a good talk! Good training during my graduate studies was essential. I had a lot of opportunities to give talks including frequently presenting to senior scientific committees at work. My mentor helped me practice and gave me tips, in addition to a course on public speaking, which helped me to not be nervous once on stage and to deliver the talk as I had prepared for it.

How was Atlanta as the host city?

The Congress Centre was well prepared for a meeting like this. It is overwhelmingly big and they were ready to host people in a structured way.

How did you navigate COVID-19 and the in-person meeting?

ASH was well prepared with outstanding access to onsite testing, great compliance with masks, which altogether created a safe environment. This setup really set the tone for the future of hybrid conferences, demonstrating how these arrangements work well. It was also amazing to get to see ISEH members in person and to bring the ISEH community together at this meeting.

Summary and next steps for ISEH 2022

In total, around 13,250 people joined ASH 2021 in person and an additional 16,550 online. The hybrid format was crucial for those unable to travel due to ongoing travel restrictions at the time, and to increase accessibility to those unable to fund expensive travel to the US.

The ASH virtual platform provided many opportunities for interaction with the speakers and other attendees, such as the ASH internal networking platform, interactive sessions such as “Meet-the-scientist” and live Q&A. All of those options helped engage the only-virtual audience in the meeting.

However, going back to “in-person hematology” highlighted the importance of in-person meetings, where many interactions occur through casual lunches, drinks during the poster session and afternoon coffees. Those types of interactions are still difficult to replace by current online platforms.

We hope that the success of the ASH hybrid meeting will pave the way for the upcoming ISEH 2022 Annual Meeting, which will also be held in a hybrid format in Edinburgh in September 2022. Looking to learn more about ISEH's hybrid approach and our scientific meeting content for ISEH 2022? Visit www.iseh.org/iseh2022 to learn more and register today!

Blog post contributed by:
Kristina Kirschner, PhD - @krikirschner
Group Leader, Institute of Cancer Sciences/ CRUK Beatson Institute
University of Glasgow, Scotland

Alba Rodriquez Meira - @AlbaRMeira

Sir Henry Wellcome Fellow, Dana Farber Cancer Institute
Cambridge Stem Cell Institute, United Kingdom

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Each month, Simply Blood spotlights a lab contributing to the fields of hematology, immunology, stem cell research, cell and gene therapies, and more. Get to know groups doing cutting edge research from around the world! This month, we are featuring the Vanuytsel Lab which is based out of the Center for ⋯

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