GDCB Seminar

4:10 p.m. • Tuesday, Jan. 18, 20221 • 1414 Molecular Biology Building

'The long and winding road: hematopoietic formation to function'

Abstract: Hematopoietic stem cells (HSCs) arise embryonically and sustain the entire blood system from birth until death due to their immense capacities for self-replication and multi-lineage differentiation. Accumulation of malfunctioning HSCs results in hematologic disorders such as clonal hematopoiesis, myelodysplastic syndrome (MDS), and acute myeloid leukemia. Our group seeks to define regulators critical for de novo HSC production using genomics approaches and genetic manipulation in embryonic zebrafish and decipher how mutations found in human MDS alter stem cell traits and influence differentiation choices. Our recent studies in early development revealed that nascent HSCs robustly regenerate but display differentiation latency until later in life. In contrast, HSC-independent embryonic progenitors, which arise concurrently with HSCs, sustain hematopoiesis from embryonic until juvenile stages, much later than previously expected. We also discovered that the MDS-associated factor DEAD-box helicase 41 (Ddx41) is a novel regulator controlling the number of hematopoietic stem and progenitor cells (HSPC) emerging during development. Deficiency of Ddx41 results in accumulation of R-loops, nucleic acid structural variants comprised of ssDNA and RNA: DNA hybrids, which serve as stimulants of the cGAS-STING inflammatory cascade that can promote HSPC production. Combined, our studies have implications for unlocking the programs underlying the genesis of bona fide HSCs and deciphering mechanisms that drive their aberrant expansion in myeloid malignancies.

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Host: Raquel Espin Palazon, genetics, development and cell biology assistant professor