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POSTER 6: Decoding the molecular role of the aorta microenvironment in HSC generation

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Hematopoietic stem cells (HSCs) are a rare population of cells responsible for all blood cells production. HSCs appear at a specific time during embryo development from a subset of endothelial cells (ECs) called hemogenic endothelial cells (HECs), within the aorta-gonadmesonephros region. HECs will ultimately undergo endothelial-to-hematopoietic transition (EHT) to generate HSCs. In human, as in avian embryos, HEC specification is restricted to the ventral side of the aorta and this dorso-ventral polarization is mainly resulting from molecular signals coming from the surroundings of the aorta. How the anatomical structures (notochord, gonads/mesonephros ...) and their associated molecular signals restrict the emergence of HECs to the floor of the aorta are still poorly investigated. To address this question, we are using the chicken embryo because it allows in ovo manipulation and micro-surgery approaches. We are altering the dorso-ventral polarity of the aorta before HEC specification by: 1. removing surgically the dorsal structures, i.e., the notochord and the neural tube; and 2. grafting ventral structures, such as the intermediate mesoderm (the precursor of the gonads/mesonephros) in place of the dorsal structures. We exploited the consequences of the ablations/grfts by quantifying HEC specification and hematopoietic cell commitment using RUNX1 (a transcription factor specifying HEC commitment and controlling EHT) and CD45 immuno-stainings, respectively. After ablation of the dorsal structures, we observed: 1. HEC specification occurring more laterally in the aorta and 2. a massive ectopic specification of HECs dorsally when ventral structures were grafted. We will take advantage of this challenging and unprecedented in vivo experimental design to decipher the main key molecular players that are coming from the microenvironment of the aorta using spatial transcriptomic technology. Taken together, this study will provide a better understanding on the molecular regulations leading to HSC generation.

