Exploring ZEB-1 interactome in Endothelial cell signalling

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Lymphangiogenesis (the formation of lymphatic vessels) is inevitably crucial during development and provides an alternative route for tumor metastasis. Endothelial cells constitute the supportive luminal lining of blood and lymphatic systems throughout the body. Sharing a common origin, a growing interest has been drawn toward the molecular pathways involved in the process pinpointing the resemblance to the process of angiogenesis. Nevertheless, the significant molecular discrepancies are yet to be revealed. Recently, we have shed the light on the potential role of ZEB-1 in angiogenesis.

In this perspective, we investigated its relevance in lymphangiogenesis. Silencing ZEB-1 by RNA interference was used to determine ZEB-1 regulated proteome in Human Dermal Lymphatic Endothelial Cells (HDLECs). Indirect immunopreciptation was performed pulling down ZEB-1 in HDLECs and Human Umbilical Vein Endothelial Cells (HUVECs), which is further investigated by probing for potential binding partners using western blotting.

Here, we found that knocking down ZEB-1 significantly affects invitro expression of key components in lymphangiogenesis associated signalling pathways. For instance, silencing ZEB-1 significantly decreases invitro expression of Yes-associated protein-1(YAP-1), a key component of the Hippo pathway (decreased by 71% ± 6.6% of non-silencing control, $p<0.05$). In addition to our knockdown data, immunopreciptation of ZEB1 revealed potential interaction with YAP-1 in HDLECs and HUVECs. YAP-1 was reported to negatively Prox1 in developmental and pathological lymphangiogenesis. Additionally, interactions with members of activator protein-1 (AP-1) transcription factor family, FOSL-1, FOSL-2 and c-Jun have been observed. Intriguingly, ZEB-1 showed a promising interaction with PRH, a transcription factor known to directly interact with Prox1.

Collectively, we have identified the involvement of novel unravelled ZEB-1 binding partners which have been shown to have pivotal roles in the process of lymphangiogenesis and angiogenesis.