Within the *blood vessel* network, nine of IL-1β's top 20 neighbors are not top neighbors in the tissue-naïve network. Eight of these genes are transcriptionally regulated in vascular cells based on IL-1β treatment (Fig. 2b). For example, MCL-1 is an anti-apoptotic gene involved in survival of endothelial cells[1,2]. It is rapidly induced by growth and inflammatory stimuli in vascular cells[3,4] to control vascular apoptosis[5]. PAI-1 (also called SERPINE1) is produced and secreted by vascular cells[6] in response to various agonists such as hormones, growth factors, endotoxin, cytokines and phorbolesters[7]. Specifically, IL-1β increases PAI-1 mRNA and protein expression in a dose- and time-dependent manner in endothelial cells[8]. PAI-1 plays an important role in several vascular pathologies, including atherosclerosis and vascular remodeling[6,9]. TNFAIP2 (also B94) is known as a primary inflammatory response gene induced in endothelial cells by inflammatory stimuli, including IL-1β[10]; it is also induced in endothelial progenitor cells involved in vascular repair[11]. Chemokines CXCL2 (GRO-beta) and CXCL3 (GRO-gamma) are known to function in the endothelial inflammatory response[12–16]. A20 (also known as TNFAIP3) is induced in response to injury and to inflammatory stimuli in vascular cells[17]. A20 is involved in neovascularization that is strongly induced by and plays a role downstream of IL-1β in vascular endothelial and smooth muscle cells[17–19]. Inflammation-induced IER3/IEX-1[20] plays a role in vascular endothelial and smooth muscle physiology and cardiovascular disease[21–24]. IL-8 is involved in the establishment and preservation of the inflammatory microenvironment of the blood vessel, and is implicated in cardiovascular diseases including atherosclerosis, hypertension and coronary artery disease (CAD)[25].

The ninth gene, GLIPR1, does not show a transcriptional response but is among the top genes linked to IL-1β in the *blood vessel* network. GLIPR1 belongs to the CAP superfamily, several members of which are involved in innate immune response[26,27], and has links to endothelial inflammatory modulation[28–30] and angiogenesis[31]. GLIPR1 has been shown to be regulated post-transcriptionally, potentially via subcellular localization[32], and thus lack of differential expression in steady state levels of its mRNA might not be unexpected. This is similar to what we observe for IL-1R, the receptor for IL-1β, which is internalized upon treatment and precedes IL-1β induced gene-expression[33]. Altogether, this demonstrates that tissue-specific functional networks discover both tissue-specific transcriptional and post-transcriptional regulatory responses.

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