**EMERGING MOLECULAR MECHANISMS OF PULMONARY ARTERIAL HYPERTENSION: ARE WE CLOSER TO A CURE?**

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Pulmonary arterial hypertension (PAH) is a devastating disease that affects people of all ages, but particularly young women, and is a progressive and often lethal disease. Despite many recent therapeutic advances, most patients ultimately progress and the prognosis remains poor with a mean survival of only 3-5 years after diagnosis. Increasingly, evidence is pointing to endothelial cell (EC) apoptosis as a critical trigger in the pathogenesis of PAH. Loss-of-function mutations in the bone morphogenetic protein receptor 2 (*Bmpr2*) genes have been linked with familial PAH, and this receptor has been recently shown to mediate EC survival signaling. As well, inhibition of the VEGF receptor 2 with SU5416 coupled with hypoxia exposure results in widespread EC apoptosis producing a severe and progressive form of PAH exhibiting pathological lesions characteristic of the clinical disease. We tested whether EC apoptosis is sufficient to induce PAH and complex lung vascular remodelling by creating a transgenic mouse model overexpressing an artificial Fas-inducing apoptosis (FIA) transgene under the control of an endothelial-specific promoter, activated by a small molecule dimerizing agent. Indeed, this endothelial FIA (EFIA) model exhibited dose-dependent increased in right ventricular systolic pressure (RVSP) in response to the dimerizing agent, as well as highly proliferative lesions tightly associated with small lung arterioles. As well, proteomic analysis of blood outgrowth ECs from patients with BMPR2 mutations and PAH, compared to control cells revealed the differential expression of a number of proteins involved in the regulation of EC growth and survival, which may provide novel targets for therapeutic interventions.