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Contribution of genes in the development of pulmonary hypertension

Genes involved in idiopathic pulmonary hypertension were further described by Professor Trembath. The known defects in IPAH are located on BMPR II as mentioned previously, and on Alk I and 5-HHT. Knockout mice for BMPR II can not survive but +/- phenotypes have some features of IPAH on the pulmonary vasculature and the right heart. A large study on 210 patients with IPAH has shown a wide array of mutations on BMPR II, most of them being on the kinase domain, on the extracellular and lastly cytoplasmic domains. BMPR II plays a crucial role on cell transcription regulation. In IPAH, the BMPR II mutations lead to markedly reduced lung BMPR II in tissue section. The combined finding of hereditary haemorrhagic telangiectasis with pulmonary hypertension has allowed the discovery of Alk I mutation on endothelial cells, genes playing also a crucial role on smad 2, 3 and 4, with antiproliferative effects on pulmonary vascular cells. All together, the identified genetic defects barely account for 50 % of identified IPAH and their presence does not allow to predict the incidence of the disease sufficiently to justify nowadays systematic genetic counselling in IPAH , but systematic genetic research is needed.

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Chairman of the session "Epidemiology and genetics of pulmonary hypertension"