Quantification of the proteomic signatures underlying human placental vascular maturation.

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Fetal growth is dependent upon the appropriate maturation of the placental vasculature yet the molecular signatures underpinning this process in humans remain unresolved. In an effort to address this, we used a proteome-scale approach (LC-MS-based, label-free quantification of trypsin-treated homogenates using SWATH) to investigate the protein expression changes accompanying placental chorionic plate artery development between 1st (7-12 weeks, n=9) and 3rd (39-40 weeks, n=7) trimesters of normal pregnancy (LREC 10/H0906/71). 3586 distinct proteins were quantified on the basis of at least two unique peptides identified per protein. Dynamic regulation of the placental vascular proteome was evident with 1539 proteins differing significantly between 1st and 3rd trimester (t-test with multiple comparison correction, FDR <0.05). 710 proteins were up-regulated at term and pathway analysis revealed many notable features to be indicative of vascular maturation. Examples of these were: (i) The down-regulation of molecules key to gene splicing and protein synthesis. These included 41 spliceosome proteins (e.g. top-regulated, ACIN1), 68 ribosomal proteins (e.g. RPL10A) and 18 translation initiation/elongation factors (e.g. ELF4A3). (ii) The up-regulation of components of myofilament/cytoskeletal integrity and metabolic-contraction coupling. These included 31 focal adhesion-related proteins (e.g. FLNA), 13 LIM domain proteins (e.g. PDLIM3) and all elements of the glycolytic cascade (e.g. GP1). Our study gives a comprehensive description of the major protein expression changes, and underlying biological processes, associated with human placental vascular maturation. This also provides a valuable resource to investigate if these features are altered in situations of compromised fetal growth.

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