Placenta growth factor (PIGF) is a member of the PDGF/VEGF family of growth factors that share a conserved pattern of eight cysteines (1-3). Alternate splicing results in at least three human mature PIGF forms containing 131 (PIGF-1), 152 (PIGF-2), and 203 (PIGF-3) amino acids (aa) respectively (1-3). Only PIGF-2 contains a highly basic heparin-binding 21 aa insert at the C-terminus (1). In the mouse, only one PIGF that is the equivalent of human PIGF-2 has been identified (3). Mouse PIGF shares 60%, 92%, 62% and 59% aa identity with the appropriate isoform of human, rat, canine and equine PIGF. PIGF is mainly found as variably glycosylated, secreted, 55-60 kDa disulfide linked homodimers (4). Mammalian cells expressing PIGF include villous trophoblasts, decidual cells, erythroblasts, keratinocytes and some endothelial cells (1,5-7). Circulating PIGF increases during human pregnancy, reaching a peak in mid-gestation; this increase is attenuated in preeclampsia (8). However, deletion of PIGF in the mouse does not affect development or reproduction. Postnataally, mice lacking PIGF show impaired angiogenesis in response to ischemia (9). PIGF binds and signals through VEGF R1/Flt-1, but not VEGF R2/Fk-1/KDR, while VEGF binds both but signals only through the angiogenic receptor, VEGF R2. PIGF and VEGF therefore compete for binding to VEGF R1, allowing high PIGF to discourage VEGF/VEGF R1 binding and promote VEGF/VEGF R2-mediated angiogenesis (1,5,9,10). However, PIGF (especially human PIGF-1) and some forms of VEGF can form dimers that decrease the angiogenic effect of VEGF on VEGF R2 (4, 5). PIGF-2, like VEGF164/165, shows heparin-dependent binding of neuropilin (Npn)-1 and Npn-2 and can inhibit nerve growth cone collapse (11,12). PIGF induces monocyte activation, migration, and production of inflammatory cytokines and VEGF. These activities facilitate wound and bone fracture healing, but also contribute to inflammation in active sickle cell disease and atherosclerosis (6,7,9,13-16). Circulating PIGF often correlates with tumor stage and aggressiveness, and therapeutic PIGF antibodies are being investigated to inhibit tumor growth and angiogenesis (5,13).

References: