Effects of Obesity on Angiogenesis and Regenerative Lung Growth

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Introduction: Obesity is associated with the impairment of wound healing and tissue regeneration. Angiogenesis, the formation of new blood capillaries from preexisting blood vessels, plays a key role in organ regeneration and repair. Inhibition of angiogenesis attenuates lung growth after unilateral pneumonectomy (PNX) and obesity is accompanied by endothelial cell dysfunction. This project aims to investigate the effects of obesity on post-PNX lung vascular and alveolar morphogenesis. **Methods:** We perform PNX on leptin-deficient (*Lep*$^{ob/ob}$) mice under a 10% high-fat diet and investigate the effects of obesity on angiogenesis and regenerative lung growth using biochemical and immunohistochemical analysis. **Results:** Post-PNX regenerative lung growth is inhibited in *Lep*$^{ob/ob}$ obese mice compared to *Lep*$^{ob/+}$ mice. The levels of the major angiogenic factor, vascular endothelial growth factor (VEGF) are higher in the serum and the lung tissue collected from post-PNX mice compared to those from sham-operated control mice, while these effects are attenuated in post-PNX *Lep*$^{ob/ob}$ mice. The levels of adiponectin, one of the adipokines that exhibits pro-angiogenic and vascular protective properties, increase in the remaining mouse lungs after unilateral PNX, while these effects are attenuated in *Lep*$^{ob/ob}$ obese mice. Regenerative lung growth, vascular and alveolar morphogenesis, and VEGF levels in the post-PNX mouse lungs are inhibited in adiponectin knockout mice. **Conclusions:** These results suggest that obesity inhibits post-PNX regenerative lung growth through adiponectin-VEGF signaling. Modulation of adiponectin-VEGF signaling may be an efficient strategy to restore lung regeneration and repair in obese people.