Anti-Endoglin Antibodies and Mice Expressing Novel Human/Mouse Chimeric Endoglin
Ref# RP11-001

Keywords: Human endoglin gene (hENG), immunoconjugate, leukemia, angiogenesis, vascularization.

Collaboration Research Opportunity: Roswell Park Cancer Institute is seeking partners to help co-develop novel human/mouse chimeric endoglin models for prophylaxis and therapy of angiogenesis associated disease.

Summary: Endoglin is a homodimeric tumor-associated cell membrane antigen that is mainly expressed on leukemia cells and endothelial cells. Endoglin’s expression on endothelial cells is upregulated on proliferating endothelial cells of the tumor-associated vascular and lymphatic endothelium. Endoglin is also essential for angiogenesis and vascular development. Endoglin has an extracellular region, a hydrophobic transmembrane region, and a cytoplasmic tail.

Although human and mouse endoglin, appear very similar in the transmembrane and cytoplasmic regions, there is substantial difference in the extracellular region. It has been observed that these differences in human and murine extracellular regions would be sufficient for generating distinct antigenic epitopes unique to human or mouse endoglin. By the use of anti-endoglin antibodies and various staining procedures it has been determined that endoglin is expressed at moderate levels on human tumor cells such as from leukemias. In addition, it has been determined that endoglin is expressed at moderate to high levels in endothelial cells contained in tumor-associated vasculatures from solid tumors as well in pathological conditions involving angiogenesis.

There is a need for antiangiogenic therapy to inhibit tumor angiogenesis that would suppress or arrest tumor growth and its spread. There is also a need for new animal models expressing human endoglin that can be targeted by more anti-human endoglin mAbs, as well as a need for new effective anti-human endoglin mAbs themselves.

Technology: This technology provides novel knock-in mice which in turn express novel human/mouse chimeric endoglin. The mice are useful for evaluation of the in vivo efficacy of anti-human mAbs which can be used in anti-angiogenic therapy of human tumor angiogenesis and human angiogenesis-associated diseases characterized at least in part by excessive vascularization. The endoglin gene of the knock-in mice comprises exons 4,5,6,7, and 8 and combinations thereof of the human endoglin gene (hENG). The mAbs do not cross-react with murine endoglin, and are specific for portions of hENG.

The invention also provides methods for using the anti-endoglin mAbs for prophylaxis or therapy of human tumor angiogenesis and for angiogenesis-associated diseases having excessive vascularization. In general, the method comprises administering a composition of one or more of the mAbs, hENG binding fragments, and/or immunoconjugates developed from the mAbs.

Potential Commercial Applications:
- To help identify potentially new anti-endoglin monoclonal antibodies that can be useful for therapeutic applications to cancer patients.
This technology could help determine effective combinations of anti-endoglin monoclonal antibodies with other agents for effective combination therapy of cancer. 

Could provide methods for using anti-endoglin mAbs for prophylaxis or therapy of human tumor angiogenesis and for angiogenesis-associated diseases having excessive vascularization.

**Competitive Advantages:**

- This technology helps to overcome non-reactivity that is seen in most anti-hENG mAbs which do not react with mouse ENG or mouse endothelial cells.
- This technology also overcomes concern on whether animal models would suffer from defective vascular development or hereditary hemorrhagic telangiectasia-like symptoms.
- Epitopes defined by these mAbs have been mapped, thus this mouse model will be useful for evaluating anti-tumor efficacy of many anti-hENG mAbs.

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