Development of an Antibodies Phage Display System for Studying Angiogenesis

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Angiogenesis is the formation of new blood vessels from pre-existing one and is an important physiological process, which in adults is mostly restricted to wound healing or the female reproductive cycle. However, many disorders, such as cancer or retinopathies, induce the formation of pathological angiogenesis, necessary for disease progression. Because the vascular endothelial growth factor (VEGF) is the main molecular factor responsible for the formation of new blood vessels, most of the angiogenic drugs available in the clinic today are directed against VEGF or its receptors. However, although anti-VEGF therapies are effective, they are not yet ideal due to undesirable side effects and drug resistance. Novel alternatives are necessary to improve on angiogenic therapies. The aim of our study is to identify novel molecular targets and to develop new therapeutic agents for angiogenic dependent diseases. To achieve our goal we have chosen the phage display system in order to select for antibodies with angiogenic properties. Two antibody phage libraries are being developed in our laboratory, directed against VEGF and human endothelial cells. The animals were immunized and developed specific antibodies, detected by ELISA and Western-blot. Amplification of the pool of light and heavy chain Ig genes was performed to produce the single chain (ScFv) fragments for library construction. The ScFv antibody display libraries will be then screened in angiogenic settings to isolate antibodies against specific VEGF isoforms and novel cell surface molecular markers expressed by activated human endothelial cells.

Keywords: Phage Display; Monoclonal antibodies; VEGF

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