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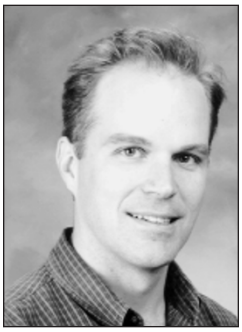

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1985-1986	Chemical Engineer, E.I. DuPont de Nemours, Newark, DE
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Co-inventor on four published patents, over 50 published papers

Targeting Adenovirus Vectors

Increasing the tissue selectivity of adenovirus for gene therapy has the potential to make these therapies safer, reduce humoral and CTL response against Ad, and to better enable the systemic administration of Ad. The development of tissue selective adenovirus requires the generation of adenovirus vectors which lack native receptor binding and additionally contain domains which redirect the vector to tissue-specific receptors. Towards this goal we have succeeded in delineating the CAR-binding domain on the adenovirus fiber knob through the identification of several mutations in the knob protein which ablate binding to CAR. However, to overcome the resultant hurdle of growing CAR-ablated vectors, we have developed a cell line, 293-HA, expressing an alternate "pseudoreceptor". This pseudoreceptor is comprised of a receptor transmembrane domain fused to a single-chain antibody which recognizes the HA peptide epitope. The anti-HA pseudoreceptor is able to mediate the binding and uptake of tropism-restricted vectors which incorporate the HA epitope into either the fiber or penton base coat proteins. Using this cell line we have succeeded in creating adenovirus vectors which lack all known native receptor binding. With the native tropism of Ad completely ablated in these vectors, a target receptor validation technology will be discussed which allows the rapid determination of the feasibility of targeting different receptors using these vectors.