Targeted, virus mediated gene delivery holds the potential to treat previously un-curable diseases. Gene delivery to the common blood progenitor cells located in bone marrow, hematopoeitic stem cells (HSCs), can provide a life-long source of a gene, therefore, a single injection may last a lifetime. To date, there are no publications claiming to successfully specifically target human primary HSCs in vivo or in vitro via the CD34 receptor, the sole reliable marker for human HSCs. Viral vectors are among the most efficient gene delivery machines. Recently, our group developed a new method to target genes to specific cell types in vivo using lentivectors (Yang et. al., 2006, PNAS 103:11479-11484). In order to target and deliver a gene using a lentivirus, cell binding and fusion must occur. Usually, binding and fusion are coupled at the same glycoprotein. Most previous attempts at targeted gene delivery have involved manipulating this glycoprotein by inserting targeting molecules into different locations within this glycoprotein or adding a ligand or antibody to bridge the virus to the cell. These methods have resulted in low viral titer, most likely due to the interruption of the natural binding or fusion of the virus, and are unacceptable for therapeutic applications. However, separating binding and fusion allows for increased specificity without decreasing the titer. Using an anti-CD34 antibody as a targeting molecule and a binding-deficient, fusion competent mutant of the Sindbus virus glycoprotein as a fusogen, we have been able to specifically target CD34+ cell lines both in vitro and in vivo. We have further shown that both the antibody and fusogen are required for infection. We are planning to test primary CD34+ cell targeting in vitro and eventually in vivo in a humanized mouse model.

Reference:
Yang, L., Bailey, L., Baltimore, D., & Wang, P. (2006) *Proc. Natl. Acad. Sci. USA* **103**, 11479-11484.