Understanding the Effects of siRNA Knockdown of ErbB Receptors on GGF2 Signaling Potency

Cain, Evan

Heart disease is the leading cause of death in the U.S., and in 2013 was responsible for 611,105 fatalities, according to the CDC. GGF2 is a neuregulin-1, Type II protein isoform that mainly signals through the ErbB3 and ErbB4 receptors of the ErbB family of receptor tyrosine kinases. GGF2 has been isolated because of its ability to induce cardiomyocyte proliferation and differentiation. Whereas current therapies seek to compensate for a heart's diminished pumping ability in patients with heart disease, this biologic therapy would offer the prospect of physically repairing heart tissue. In order to better understand the signaling characteristics of GGF2, and with the help and support of my mentor, cell lines representing liver (HepG2), breast (MCF-7), and cardiac (HL-1) tissue were transfected with siRNA for various durations in order to knockdown the expression of various ErbB receptor subtypes. Following GGF2 treatment, ErbB quantification analyses via a Wes™ assay were performed to ensure ample knockdown. A p-AKT assay was then performed on the transfected cells in order to model their dose responses to GGF2. The data obtained suggested that GGF2 was most dependent upon ErbB3-mediated p-AKT formation in vitro. These results not only facilitate a better understanding of ErbB-GGF2 signaling across these cell lines, but also suggest that mutation of the EGF-like domain of the GGF2 molecule to have a greater affinity for ErbB3 receptors could ultimately optimize signaling potency and treatment efficacy.

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