**Identification of selective DDR1 Kinase Inhibitors using Structure activity relationship**

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Discoidin domain receptor 1 (DDR1) is a receptor tyrosine kinase that binds to and is activated by collagens. Although activation of DDR1 is required for normal tissue development, DDR1 upregulation and/or activation following injury is detrimental in conditions such as cancer, atherosclerosis, and fibrotic diseases. The focus of our research is to determine the role of DDR1 in kidney fibrosis. We showed that loss of DDR1 reduces fibrosis and improves renal function in models of kidney disease. In addition, cells expressing kinase dead DDR1 produce significantly less collagen than cells expressing wild type DDR1. This result indicates that the kinase activity is required for DDR1-mediated pro-fibrotic effect. Based on this finding, our goal is to develop a small molecule ATP-competitive inhibitor that can selectively inhibit the kinase activity of DDR1. Using structure-activity relationship optimization and time-resolved fluorescence energy transfer assays, we synthesized and screened 95 derivatives of a previously characterized inhibitor, Compound 1 (IC50 for DRR1 = 11.9nM), in order to generate inhibitors with better selectivity and lower IC50. Because of the high homology between DDR1 and DDR2, we tested potential inhibitors for selective inhibition of DDR1 versus DDR2. Our results revealed 14 promising inhibitors, three of which showed a lower IC50 than Compound 1. However, all 14 small molecules inhibited both DDR1 and DDR2. We are in the process of refining the structures of the 14 compounds to improve selectivity and specificity. Our ultimate goal is to use these inhibitors in the setting of fibrotic diseases.

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