Small Molecule Inhibition of Discoidin Domain Receptor 2

Background:
Breast cancer is predicted to kill approximately 41,000 women in 2017 alone, and more than 90% of these women will die from metastatic disease. While the exact mechanisms of tumor metastasis have yet to be fully determined, increased collagen deposition in breast tumors has been implicated with more invasive tumors and a poorer prognosis. A collagen-induced receptor tyrosine kinase, discoidin domain receptor 2 (DDR2), has been observed to be prevalent on the leading edges of breast cancer tumors. Though unexpressed by normal breast tissue, 50-70% of breast tumors express DDR2, and DDR2 is critical for breast cancer metastasis in murine models.

Technology Description:
DDR2 can be selectively inhibited by a potent small molecule, which blocks the extracellular collagen binding domain. Tyrosine kinase inhibitors (TKIs) are used widely as chemotherapy agents, due to the role of tyrosine kinases in cell growth signaling. However, inhibition of the kinase domain of DDR2 is not selective and therefore subject to off-target effects. The selectivity and potency thus makes this small molecule an attractive treatment option for tumor metastasis. Existing compounds in clinical use have been demonstrated to inhibit DDR2, but these compounds are multi-targeted and may not be effective at safe doses.

Advantages:
- Inhibition of metastasis-associated receptor tyrosine kinase (DDR2)
- Highly selective method of targeting DDR2
- Potential prevention of breast tumor metastasis
- Opportunities to treat metastasis in multiple cancer types


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Application Space
Cancer therapeutics, Drug discovery