Docket #: S10-397

Scaffold-kinase interaction blockade for treatment of RAS/MAPK-Pathway driven cancers

Researchers in Prof. Paul Khavari's laboratory have discovered a novel compound and method to block invasive neoplasia without effects on normal cells. This technology targets a small domain (WW domain) of a scaffolding protein (IQGAP1) that binds proteins in the Ras/MAP kinase-signaling pathway. The Ras-Raf-Mek-Erk MAPK pathway is implicated in >40% of all human cancers, but targeting components of the pathway have not yielded valid therapeutics due to the risk of side effects on normal cells and mechanisms of acquired resistance. Targeting scaffold proteins rather than the canonical kinases provides a unique approach to develop therapies to treat a range of solid tumors without affecting homeostasis of normal tissues as well as to circumvent acquired tumor resistance to kinase inhibitors.

Applications

- **Cancer therapeutic** — to prevent and/or diminish tumor formation, proliferation, and/or metastasis in >40% of all human cancers characterized as Ras-Raf-Mek-Erk MAPK pathway overexpressing.

Advantages

- **Tumor-selective** — this domain is NOT required for normal human tissue homeostasis, therefore it could affect tumorigenesis without side effects on normal cells.
- **Non-toxic** — we have not observe any morbidity in WW-treated mice nor did we find anysignificant hematological or chemical abnormalities.

Publications

- Jameson KL, Mazur PK, Zehnder AM, Zhang J, Zarnegar B, Sage J, Khavari PA. IQGAP1 scaffold-kinase interaction blockade selectively targets RAS-MAP kinase-driven tumors. Nature Medicine. 2013 Apr 21.
- Patent application PCT/US2012/032375: Scaffold-Kinase Interaction Blockades and Uses Thereof in Treating Cancer

Patents

- Published Application: 20140162960
- Issued: 9,155,774 (USA)

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