130 Nuclear Import (KPNB1) inhibitor

Asset Overview

Product Type	Small Molecule
Indication	Oncology
Current Stage	Lead discovery/optimization
Target (MoA)	KPNA2 & KPNA7 Inhibitor
Brief Description	Elevated expression of diverse importins and exportins (KPNA2, KPNB1, XPO1, XPO2) has been documented in many different cancer cells. Further, down-regulation of KPNA2, KPNB1 and XPO1 inhibited cancer cell proliferation. The inhibitors in development can selectively inhibit KPNA2/7 to restrict nuclear transport of cMYC and other oncogenic factors essential for robust activation of cancer cell survival signaling pathway
Organization	Center for Drug Design and Discovery

Differentiation

□ **Unmet Needs**

- Elevated expression of diverse importins and exportins (KPNA2, KPNB1, XPO1, XPO2) has been documented in many different cancer cells. Further, down-regulation of KPNA2, KPNB1 and XPO1 inhibited cancer cell proliferation

□ **Innovations**

- Best EC50 KPNA2-mNeonGreen • 2 μM • 0.2 μM MedChem - SAR
- Multiple active compounds within series
- Direct impact on KPNB1 (TSA, MST)
- Affects known KPNB1/KPNA2 cargos, e.g. cMYC, RelA, Smad2
- No cellular toxicity
- Selective impact on Th17 dependent B-cell activation

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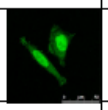
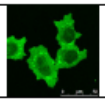
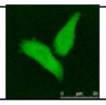
Key Data

Overview of phenotypic hit series

Overview of phenotypic hit series

	Series 21	Series 22
Phenotype KPNA2-mNeongreen 		
Best EC_{50} KPNA2-mNeonGreen	• 2 µM	• 0.2 µM
MedChem - SAR	• Multiple active compounds within series • Activity requires "warhead"	
Biophysical characterization	• Direct impact on KPNB1 (TSA, MST) • Covalent binding	• No direct impact on KPNA2/KPNB1 detected
Cargo translocation	• Affects known KPNB1/KPNA2 cargos, e.g. cMYC, RelA, Smad2 • KPNB1 interactome	• Effect on KPNB1/KPNA2 cargos
Selectivity *KPNAs* *Other Karyoph*	• Multiple KPNA's (NOT KPNA7) • No impact on TNPO1, XPO1	• Mainly KPNA2 & KPNA7 • No impact on TNPO1, XPO1
Phenotype	• Broad anti-cancer	• No anti-cancer or anti-viral activity • No cellular toxicity • Selective impact on Th17 dependent B-cell activation -
Other	• robust activity vs. cytotoxicity window	• Probe cpd synthesized • Target identification ongoing

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Intellectual Property

Patent No.	
Application Date	
Status	
Country	

Contact Information

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