Aurora Kinase Inhibitors

Aurora kinases are a class of enzymes responsible for regulating cell cycle progression. During mitosis, these proteins help facilitate chromosome segregation and cytokinesis. Aurora kinases are overexpressed in cancer cells, stimulating tumor progression; as a result, this group of proteins makes an excellent target in the development of new chemotherapeutics.

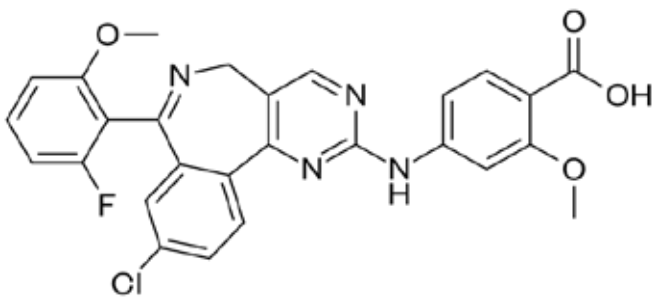
Aurora kinase A, one of three subtypes along with aurora kinases B and C, plays a signficant role in p53 signaling. The p53 signaling pathway is involved in cell growth regulation and apoptosis. The p53 protein functions as a tumor suppressor. Overexpression of aurora kinase A stimulates degradation of p53, downregulating checkpoint response signaling and facilitating oncogenic transformation in cells[1].

Aurora kinase B inhibition induces catastrophic mitosis. By preventing kinetochores from fixing inappropriate microtubule interactions, inhibition of this kinase prevents chromosome alignment and segregation, blocking cell division[2]. Aurora kinase inhibitors do not directly inhibit cell cycle progression but instead, following an aberrant mitosis, activate the p53-dependent post-mitotic checkpoint; this induces 'pseudo-G1' cell cycle arrest[3]. Because of this, highly abnormal cells continue proliferation despite the presence of significant genomic instabilities, resulting in cell death.

LKT Laboratories carries a variety of aurora kinase inhibitors. See the list below for a selection of these compounds.

Aurora kinase inhibitors:
A9714 AZD-1152-HQPA
C9708 CYC-116
G7444 GSK-1070916
M4652 MLN8237 (Alisertib)
T5996 Tozasertib
V9201 VX-11e
Z4900 ZM-447439

References:
1. Katayama H, Sasai K, Kawai H, et al. Nat Genet. 2004 Jan;36(1):55-62.
2. Ditchfield C, Johnson VL, Tighe A, et al. J Cell Biol. 2003 Apr 28;161(2):267-80.
3. Harrington EA, Bebbington D, Moore J, et al. Nat Med. 2004 Mar;10(3):262-7.



M4652 MLN8237 (Alisertib)