

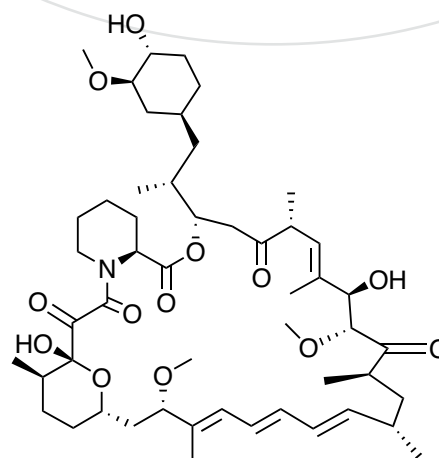
Rapamycin

Rapamycin (R0161) is an immunosuppressant traditionally used to prevent transplant rejection in organ recipients. Rapamycin suppresses mTOR signaling by complexing with FK-binding protein 12 (FKBP12) and preventing mTOR activation¹. As a result, IL-2 signal transduction is limited and B and T cell activation is inhibited.

Rapamycin also exhibits antiproliferative effects in cancer models. Proliferation of osteosarcoma cells is inhibited by rapamycin. In these cells, rapamycin induced G1 phase cell cycle arrest and autophagy; in paired animal models, it decreased growth of xenograft tumors². In breast cancer cells, this compound induced G1 phase cell cycle arrest, autophagy, and apoptosis³. When combined with **Vismodegib (GDC-0449, G1408)**, rapamycin exhibited anticancer activity in cell and animal models of biliary tract cancer. This combination decreased cell viability and proliferation and limited tumor growth⁴. In a clinical setting, rapamycin also displays chemotherapeutic efficacy. This compound decreased visceral tumor volume in subjects with tuberous sclerosis complex skin tumors⁵.

More recently, rapamycin has shown activity in models of aging and aging-related disorders. Administration of rapamycin to yeast increased

chronological life span⁶. Rapamycin's inhibition of mTOR signaling is likely responsible for the increased accumulation of storage carbohydrates and enhanced stress resistance that was linked to the increase in life span. In genetically heterogeneous male and female animal models, this compound extended median and maximal life span when administered midway through or near the end of the average murine life span⁷. Because mTOR signaling is linked to oxidative stress, the ability of rapamycin to suppress that signaling pathway and decrease oxidative stress is likely a significant factor in its ability to slow development of various diseases and, as a result, increase overall life span⁸.



R0161 Rapamycin

References:

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