

# TARGETING TPL2 IN RAS-MUTATED CANCERS

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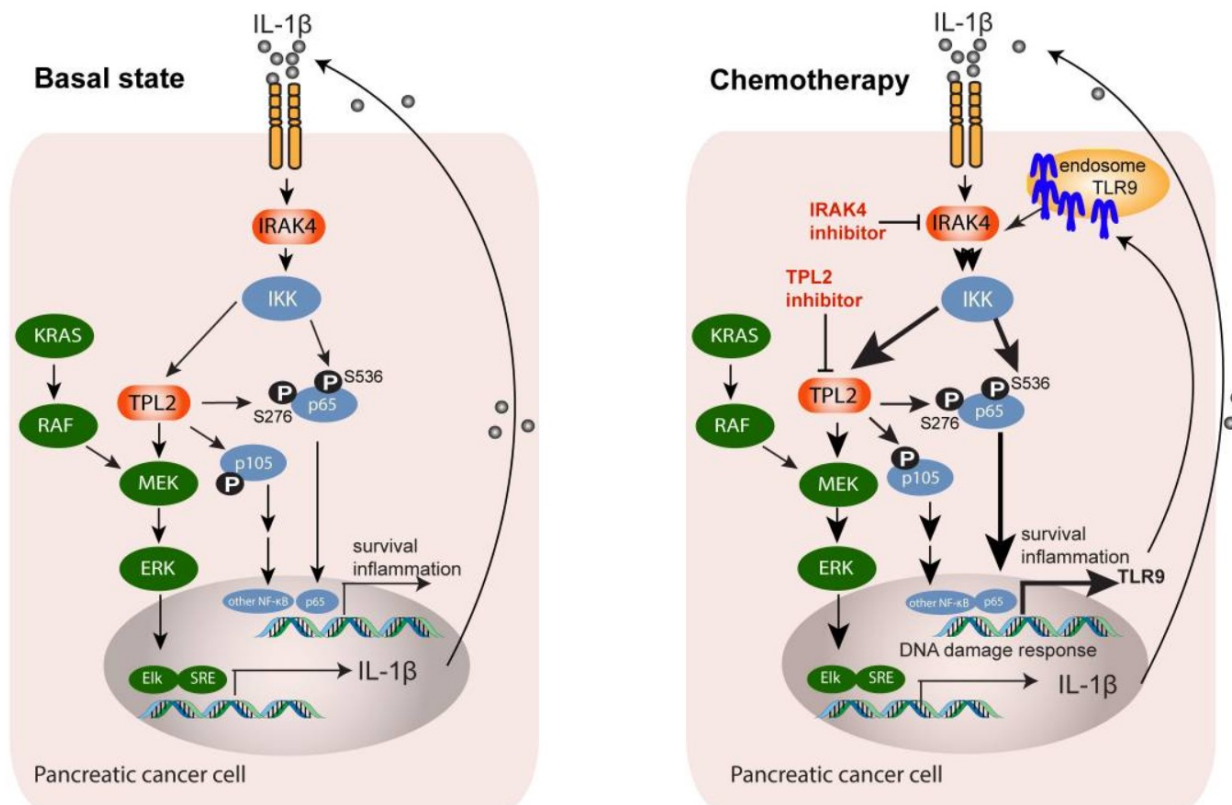
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## Technology Description

Researchers in Kian-Huat Lim's lab at Washington University have developed a therapeutic strategy to target TPL2 in RAS-mutated cancers, which should work synergistically with chemotherapy and radiation. As TPL2 (MAP3K8) is necessary for upstream activation of both MAPK and NF- $\kappa$ B signaling in RAS-mutated cancer cells, it provides a more appealing target for inhibitors than MEK/ERK or NF- $\kappa$ B alone.

In RAS-mutated cancers, inhibiting RAS-induced MAPK signaling is a common therapeutic strategy. However, tumor cells evade those therapeutics by activating NF- $\kappa$ B signaling instead, so targeting a protein upstream of both pathways represents a more effective strategy. The researchers have also identified several additional cancer types where mutated TPL2 is constitutively active.



## Stage of Research

The researchers have identified and validated TPL2 as a therapeutic target for pancreatic cancer *in vitro* using a commercially-available TPL2 inhibitor. Ongoing research involves lead generation and *in vivo* testing.

## Publications

- Dodhiawala PB, Khurana N, Zhang D, Cheng Y, ... Lin K-H. (2020). [TPL2 enforces RAS-induced inflammatory signaling and is activated by point mutations](#). *Journal of Clinical Investigation*, 130(9):4771-4790.

## Applications

- Therapeutic in RAS-mediated cancers

## Key Advantages

- Central to both MAPK and NF-κB signaling pathways

**Patents:** Pending

**Related Web Links:** Lim [Profile](#) & [Lab](#)