



The diagram illustrates the PD-1 signaling pathway and its interactions with various immune cells and tumor cells. The central focus is the T-cell, which is shown with its TCR/CD3 complex and associated signaling molecules. The pathway involves the recruitment of LCK, ZAP70, SHP-2, LAT, PLCγ1, RASGRP1, PI3K, AKT, ELK1, SKP2, CDK2, GSK3B, and FOXP3. These molecules lead to T-cell activation, proliferation, and differentiation into Th1, Th2, and Treg cells. The diagram also shows the inhibitory effects of PD-L1/PD-L2 on these cells and the role of tumor-associated fibroblasts in this process.

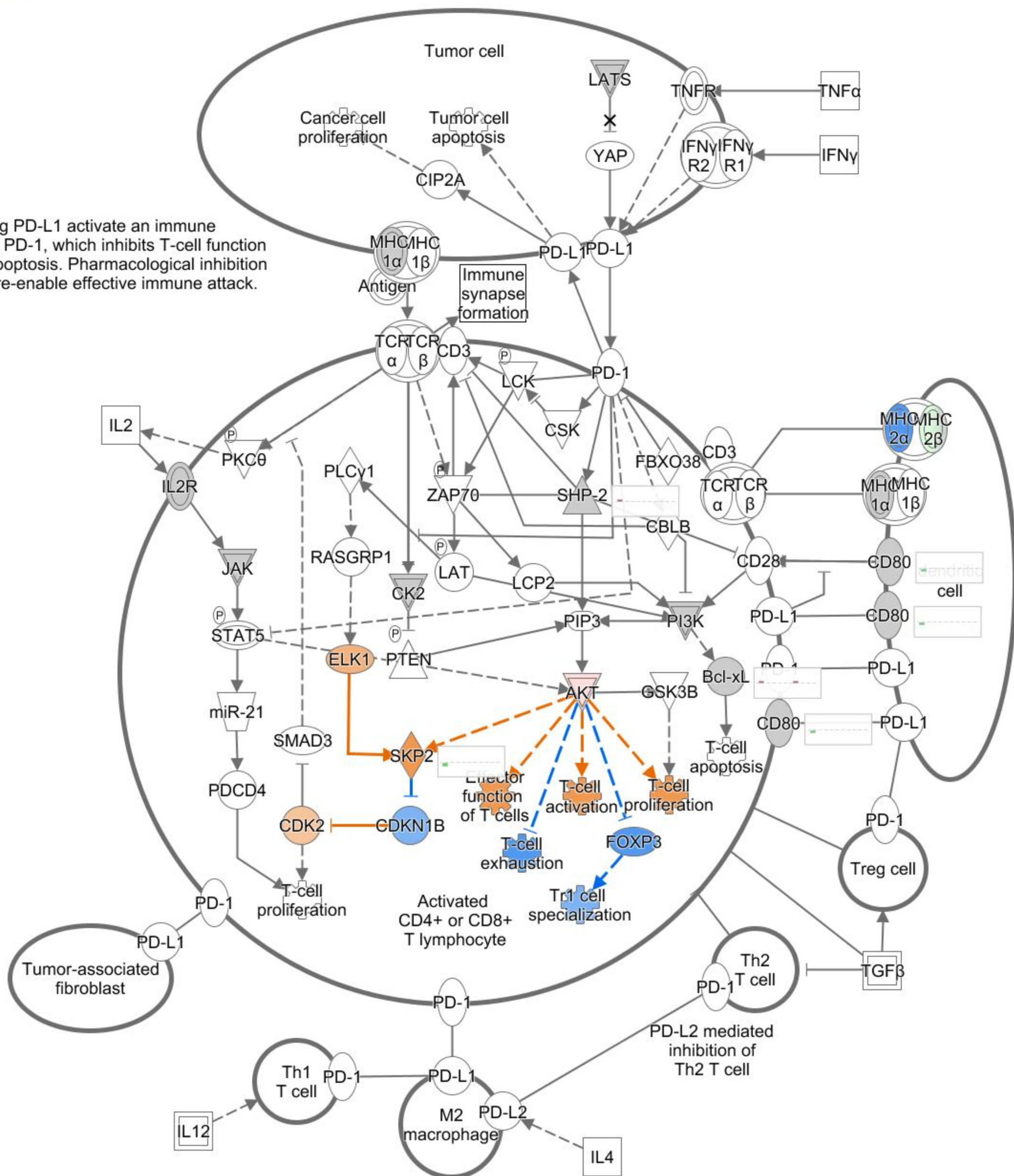
**Key components and interactions:**

- Tumor cell:** Expresses PD-L1, which interacts with PD-1 on T-cells. Tumor cell proliferation is promoted by CIP2A, and tumor cell apoptosis is inhibited by YAP.
- Immune synapse formation:** Involves MHC/HC 1α 1β, Antigen, TCR/CD3, and PD-1.
- T-cell activation and proliferation:** Initiated by the TCR/CD3 complex, leading to the activation of LCK, ZAP70, SHP-2, LAT, PLCγ1, RASGRP1, PI3K, AKT, ELK1, SKP2, CDK2, GSK3B, and FOXP3. This results in T-cell proliferation and activation.
- T-cell differentiation:**
  - Th1 T cell:** Activated by IL12, leading to the production of IFNγ and TNFα.
  - Th2 T cell:** Activated by IL4, leading to the production of IFNγ and TNFα.
  - Treg cell:** Activated by TGFβ, leading to the production of IFNγ and TNFα.
- Inhibitory pathways:**
  - PD-1/PD-L1:** Inhibits T-cell function and promotes T-cell apoptosis.
  - PD-L2:** Mediates inhibition of Th2 T cell.
  - CTLA-4:** Inhibits T-cell activation and proliferation.
  - BTLA-1:** Inhibits T-cell activation and proliferation.
  - VISTA:** Inhibits T-cell activation and proliferation.
  - HVEM:** Inhibits T-cell activation and proliferation.
  - CD28:** Promotes T-cell activation and proliferation.
  - CD80/CD86:** Promotes T-cell activation and proliferation.
- Tumor-associated fibroblast:** Expresses PD-L1, which interacts with PD-1 on T-cells, leading to T-cell inhibition.

The diagram illustrates the PD-1 signaling pathway and its interactions with various immune cells and tumor cells. The central focus is the T-cell, which is shown interacting with a Tumor cell and a Treg cell. The Tumor cell section shows PD-L1 interacting with PD-1 on the T-cell. PD-L1 is also shown interacting with TNFR and IFNγR1/IFNγR2. The T-cell section shows PD-1 interacting with TCR/CD3, LCK, CSK, SHP-2, ZAP70, LAT, LCP2, PIP3, PI3K, AKT, GSK3B, Bcl-xL, CD28, CD80, and PD-L1. The Treg cell section shows PD-1 interacting with TGFβ. The diagram also shows the effects of PD-1 on T-cell proliferation, apoptosis, and activation. Various cytokines like IL2, IL12, and IL4 are shown interacting with their receptors. The diagram is a complex network of signaling molecules and their interactions, illustrating the role of PD-1 in immune response and tumor progression.

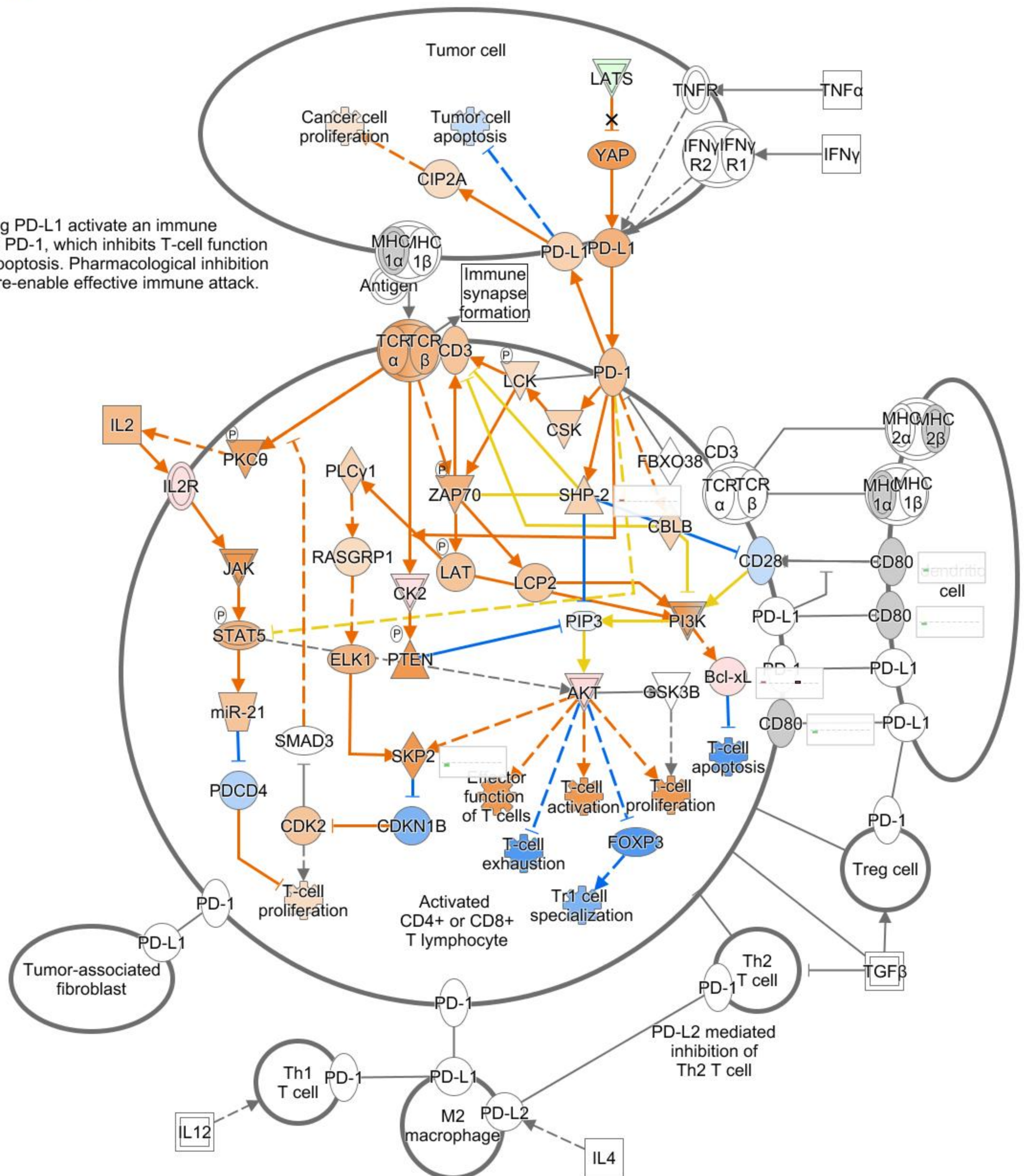
1 pM

Tumors expressing PD-L1 activate an immune checkpoint in T-cells via PD-1, which inhibits T-cell function and can even induce apoptosis. Pharmacological inhibition of the interaction can re-enable effective immune attack.



1 fM

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The diagram illustrates the PD-1 signaling pathway and its interactions with various immune cells and tumor cells. The central focus is the T-cell, which is shown interacting with a Tumor cell and a Treg cell. The T-cell's TCR/CD3 complex is activated by an Antigen presented by MHC, leading to the formation of an Immune synapse. This triggers a cascade of intracellular signals, including LCK, ZAP70, SHP-2, PI3K, AKT, and others, which ultimately lead to T-cell activation, proliferation, and specialization. The diagram also shows the inhibitory effects of PD-1 on these pathways, mediated by SHP-2 and other molecules. The T-cell's interaction with a Treg cell is shown to be regulated by TGFβ. The Tumor cell's interaction with the T-cell is shown to be regulated by PD-L1 and PD-L2. The diagram is divided into sections for Tumor cell, T-cell, and Treg cell interactions, with various cytokines and chemokines shown as modulators.

