Exploring the PD-L1 Pathway
a new direction in cancer immunotherapy research
The cancer immunity cycle

The cancer immunity cycle describes a natural process of how one’s own immune system protects the body against cancer. Cancer immunotherapy research seeks to understand how to utilize the body’s adaptive immune defense against cancer’s ability to evolve and evade destruction.

Steps 1-3: Initiating and propagating anticancer immunity
Dendritic cells capture cancer antigens and then prime and activate cytotoxic T cells.

Steps 4-5: Accessing the tumor
Activated T cells infiltrate the tumor microenvironment.

Steps 6-7: Cancer-cell recognition and initiation of cytotoxicity
T cells can recognize and kill target cancer cells, causing the release of additional cancer antigens from the tumor.
Programmed death-ligand 1 (PD-L1): an inhibitory immune pathway exploited by cancer

Cancer can evade the body’s immune response. Many tumors and tumor-infiltrating immune cells express high levels of PD-L1. Under normal conditions, the PD-L1 pathway can play an important role in maintaining immune homeostasis. In cancer, the PD-L1 pathway can protect tumors from cytotoxic T cells by disrupting the cancer immunity cycle in two ways.1-4

Within the lymph nodes

PD-L1 may inhibit cancer immunity cycle propagation in the lymph nodes

Overexpression of PD-L1 on tumor-infiltrating immune cells can prevent the priming and activation of new cytotoxic T cells in the lymph nodes and subsequent recruitment to the tumor.1-3

PD-L1 expression is upregulated on dendritic cells within the tumor microenvironment.2,3

PD-L1–expressing dendritic cells travel from the tumor site to the lymph node.5

PD-L1 binds to B7.1 and PD-1 receptors on cytotoxic T cells, suppressing activation.3

Within the tumor microenvironment

PD-L1 may inhibit cytotoxic T-cell activity in the tumor microenvironment

Upregulation of PD-L1 can inhibit the last steps of the cancer immunity cycle by deactivating cytotoxic T cells in the tumor microenvironment.1

Activated T cells in the tumor microenvironment release interferon gamma.2

As a result, tumor cells and tumor-infiltrating immune cells overexpress PD-L1.2

PD-L1 binds to T-cell receptors B7.1 and PD-1, deactivating cytotoxic T cells. Once deactivated, T cells remain inhibited in the tumor microenvironment.1,2
The PD-L1 pathway is a potential target in cancer research

Data suggest that PD-L1 may be one of the primary immunosuppressive drivers in multiple types of cancer. Inhibiting PD-L1 interactions may prevent T-cell suppression throughout the tumor microenvironment.\(^2,3\)

**PD-L1 interference affects B7.1 and PD-1 binding\(^2,3\)**
- Preventing PD-L1 from binding to its receptors on T cells may release the T cells from the inhibitory effect of PD-L1\(^1\)
- Preclinical studies suggest that preventing both interactions may propagate T-cell activity\(^2\)

**PD-L2 interactions should not be affected by PD-L1 interference\(^2,6\)**
- As suggested by preclinical studies, PD-L2 is another ligand primarily expressed on normal tissues and immune cells, protecting them during an immune response to maintain immune homeostasis\(^2,6-8\)
- PD-L1 and PD-L2 can both bind to PD-1, which may lead to T-cell deactivation\(^2\)
- Preclinical studies suggest that interfering with PD-L1 activity does not inhibit PD-L2/PD-1 interactions\(^2,6\)

PD-L1 is a potential biomarker for cancers that overexpress PD-L1

Genentech is actively investigating PD-L1 as a potential biomarker in oncology research and is committed to pursuing the potential of personalized cancer immunotherapy for cancer patients.

**PD-L1 expression has been detected on tumor cells and tumor-infiltrating immune cells\(^1,9\)**
- Tumor\(^9\)
  - PD-L1 on tumor cells (stained brown below) may lead to the inhibition of activated T cells.\(^2\)
- Tumor-infiltrating immune cell\(^10\)
  - PD-L1 on tumor-infiltrating immune cells (stained brown below) may also lead to inhibition of activated T cells.\(^2,9\)
Programmed death-ligand 1 (PD-L1): an inhibitory immune pathway exploited by cancer

- PD-L1 is an inhibitory ligand expressed by tumors and tumor-infiltrating immune cells in many cancers\(^2,4\)
- PD-L1 is a potential biomarker for cancers that overexpress PD-L1\(^2\)
- PD-L1 binding to either B7.1 or PD-1 receptors inhibits cytotoxic T cells\(^2,3\)

Discover the PD-L1 pathway, a focus of investigation and cancer immunotherapy research, by visiting Discover.ResearchPDL1.com

References: