PD-1/PDL-1 and its Potential Role in RRP
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What is PD-1/PDL-1?
Cells communicate with each other partly through proteins called ligands and receptors. A message can be sent between cells when a ligand on the surface of one cell connects with a receptor on another cell.
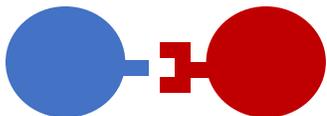

Figure 1. Ligand (blue) and receptor (red) interaction between cells.

'PDL-1' stands for 'Programmed Death-Ligand 1' and PD1 is its receptor. PDL-1 is a ligand that, when recognized by its receptor PD1, can tell the immune system not to attack. This is important for protecting the body from misdirected attacks by immune cells that can happen when the body is trying to fight off an infection. In some cases, however, tumor cells can use PD-L1 to evade the immune system and grow unchecked.

Immunology 101
The immune system allows our body to respond to foreign invaders. Two teams, the innate and adaptive, work together in the immune system. The innate team is the first line of defense – it goes after foreign invaders without much thinking. The adaptive immunity team does more work to understand who it should be attacking. This work, mostly carried out by T and B cells, takes time and results in specific targeting of foreign invaders.

The two main types of T cells are the CD4+ helper T cells and the CD8+ cytotoxic T cells. CD4+ cells are 'helpers' because they help CD8+ T and B cells adapt to fight the pathogen, or in this case tumor cells, most effectively. CD8+ T cells are 'cytotoxic' because they directly kill the bad cells.

For cytotoxic T cells to tell infected from healthy cells, they get directions from dendritic cells, which scout the body for infected cells that they ingest and break down to small pieces that are called 'antigens'. These antigens are loaded onto special surface proteins that grab the attention of cytotoxic T cells. Once the cytotoxic T cell identifies the antigen, an activation signal from the dendritic cell tells the T cell to circulate in the body and kill infected cells that match the antigen presented.[1]

PDL-1 can be found on dendritic cells, and helps tell the immune system to avoid attacking the body's own cells. Cancer cells can sometimes produce PDL-1, which tricks the immune system into ignoring them, allowing tumors to grow unchecked. In some cancers, drugs that block PD-1 or PD-L1 have been helpful for directing the immune system to attack cancer cells. [2]

PDL-1 as a Tumor Biomarker
Scientists have shown that PDL-1 is abundant on the surface of some tumor cells. PDL-1 binds the PD-1 receptor on the cytotoxic T cell, telling the cytotoxic T cell to downregulate its response to the tumor. By blocking either the ligand or receptor through immunotherapy, the inhibitory signal between the tumor cell and cytotoxic T cell can be stopped, and the cytotoxic T cell's anti-tumor response won't be downregulated. As a result, the immune response can work to target and remove tumor cells from the body.[2]
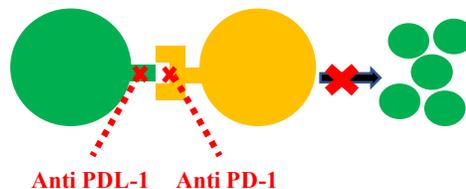

Anti PDL-1   Anti PD-1

Figure 2. Tumor cell with PDL-1 (green) and T cell with PD-1 (yellow) interact, leading to unregulated cell growth. This interaction may be inhibited by targeted therapy (red).

What Does This Mean for RRP?
Recurrent Respiratory Papillomatosis (RRP) is a condition caused by infection by HPV Types 6 and 11 that causes respiratory papillomas to grow in the airway.[3] When there is deep respiratory involvement, these premalignant papillomas have the potential for transformation to squamous cell carcinoma.[4] If the papillomas express PDL-1, the protein may be targeted by anti-PDL-1 therapy to improve the immune response against RRP.[5] This treatment should be reserved for those with severe disease, as side effects are severe and effectiveness is unknown.

Recurrent Respiratory Papillomatosis Foundation
http://www.rrpf.org
http://www.facebook.com/RRPFOrg

RRPF is a nonprofit that provides support and information for patients, family, and practitioners. This includes promotion of public awareness and aid in the prevention, cure, and treatment of RRP through encouragement and participation in promising RRP studies.

References
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