Immunotherapy, and Personalized Medicine What Do They Mean?

Community Lunch and Learn Presentation

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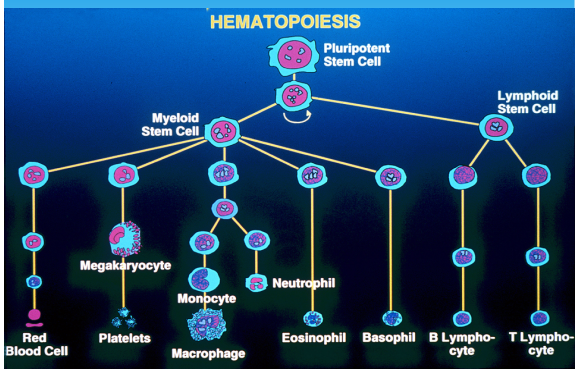
Where do these cells come from?



What is Immunotherapy?

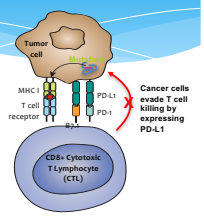
- **Immune-system based therapy** that stimulates a patient's own immune system to recognize their cancer cells and help to kill them.
- These treatments are able to induce remissions in patients with cancers without some of the complications of regular chemotherapy.
- **Such treatments are** now being offered at UNC and many other treatment centers.

Using the immune system for cancer therapy

- **Checkpoint Inhibitors**
  - Anti-PD-1 or PDL-1(Nivolumab, Pembolizumab) for lung cancer and melanomas
- **Monoclonal antibodies**
  - rituximab (CD20) for non-Hodgkin Lymphoma, trastuzumab (HER2) for breast cancer, brentuximab for Hodgkin Lymphoma
- **Adoptive T cell therapy**
  - BMT, DLI, CARs, for leukemia, lymphoma, myeloma and brain cancers

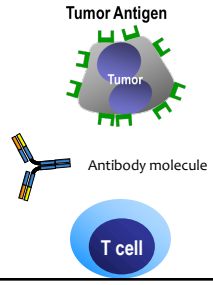
Cancer Immunotherapy with checkpoint inhibitors Like ON TV

- Cancer cells have mutations that make them recognizable by the immune system
- However, cancer cells can evade the immune surveillance by expressing proteins such as PD-L1
- Inhibiting the PD-L1/PD-1 interaction can restore anti-tumor T-cell activity, potentially leading to long-lasting responses



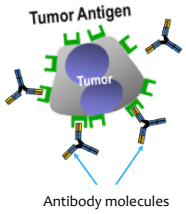
How do antibodies work?

- Tumor cells express certain proteins on their surface called tumor antigens. These proteins are like a fingerprint that identifies this cell as a cancer cell and not a normal cell
- Under normal circumstances, your body reacts against these abnormal cells by making antibodies against the cancer protein, like it makes antibodies against infections such as those bacteria that caused a "Strep throat"



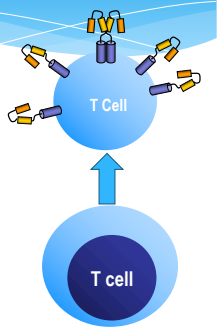
How does this work?

- Your body makes antibodies that or they can be manufactured by industry and can be administered to patients with cancer to kill the cancer cells.
- The antibodies can bind to the cancer cells and cause them to die either by starting a process of cell death called **apoptosis** or by poking holes in the cancer cell membrane.
- There are lots of drugs that are antibodies which we use to treat many kinds of cancers like breast cancer or lymphomas



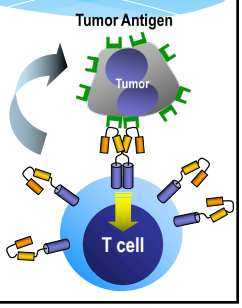
How do T cells work?

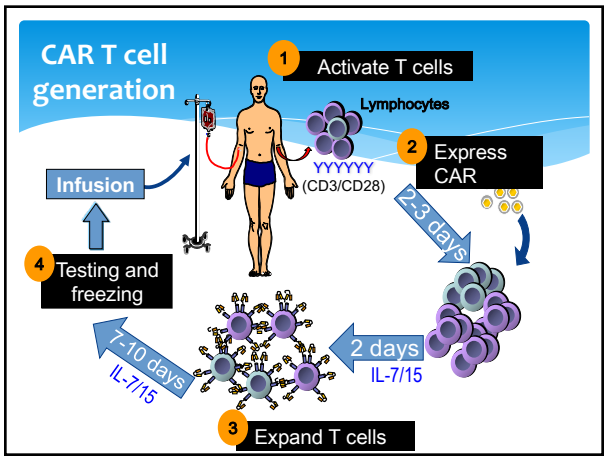
- Cancer cells are smart though, and can hide from the body's normal immune cells so they are not killed
- We now have ways of forcing the body's T cells to express the antibody proteins on their cell surface.
- This allows the "sleeping" T cells to wake up and recognize the cancer cells and then help to kill them

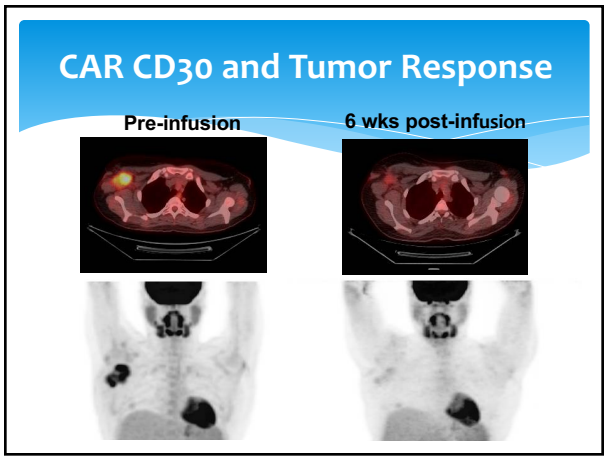


There are at least three ways for the Immune System to kill cancer cells

- Antibodies can directly kill cancer cells
- Antibodies can direct cells like T cells to kill the cancer cells
- Antibodies can allow the T cells to "unmask" cancer cells so the immune system can recognize and attack them







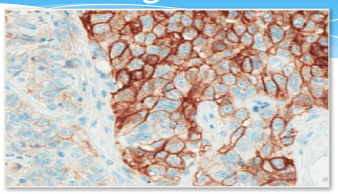
"Personalized" Medicine in Cancer

- Every cancer has specific connections or pathways inside the cells that are different or "mutated" compared to the normal cells in the organ where the cancer arose
- Many new drugs interfere with the way cancer cells grow by inhibiting the specific mutated pathways in the cell, regardless of where the cell came from. This means a "breast cancer cell" may have moved around the body and started to grow in another organ like the liver or brain.
- Sometimes these pathways lead to cells living longer and not dying like they normally do, sometimes they use cell energy differently, sometimes they don't allow the cells to degrade normal proteins like they should

Personalized Medicine

* By "sequencing" or examining how the DNA in a cancer cell is put together and comparing it with normal cell DNA, you can tell what is wrong and what "pathway" is damaged.
* If you know the abnormal pathway, then you can target it with specific drugs that are "pathway specific" rather than "cancer type specific"
* In the future we won't be talking for example about breast cancer, but a "mutated HER2neu gene" cancer or an abnormal "NF kappa B" cancer rather than a lymphoma. This knowledge will eventually allow us to pick a treatment for a cancer based on how it works at the DNA level and not based on where it came from or what it looks like under the microscope.

For Which People is Immunotherapy "The Right Stuff"

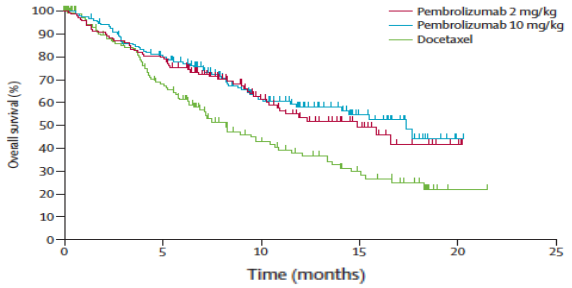


Positive PD-L1 staining in Lung Cancer

"Personalized" therapy treats ONLY those lung cancer patients with PD-L1 proteins on the surface of the tumor cell surface who are likely to benefit instead of treating everyone with lung cancer with this drug.

This "personalized" approach improves the chance of a good response to treatment and reduces the chance of side effects

Pembrolizumab in PD-L1+ NSCLC



Antibody treatment for patients whose cancers had PD-L1 on their surface lived twice as long as chemotherapy patients or those without PD-L1

Herbst et al, Lancet 2015