**JEREMY SQUIRE: EXAMPLE FAPESP PROJECT**

**TITLE: Genetic Mechanisms of Immune evasion in Prostate Cancer**

**ISSUE:**

Immunotherapy depends on tumors activating the natural anti-cancer response of our immune systems. Prostate cancer seems to have developed a way of helping it “hide” from our normal protective anti-tumor immune reactions.

**PROBLEMS**:

1) Prostate cancer responds to hormone therapies but for many men this treatment eventually stops working and they will die;

2) We do not currently have other drugs to treat aggressive prostate tumors that can kill patients;

3) Analysis of prostate tumors suggests that in some unknown way they are able to ‘turn off ’ the expression of proteins that are usually detected by our anti-cancer immune systems;

4) The global prostate cancer sequencing project has identified several genes that are often defective in aggressive prostate tumors, but the signaling effects of theses mutated genes have not been studied to see if they could be ‘turning off’ the controls of our anti-cancer immune systems.

**SOLUTIONS:**

1) There four genes (PTEN, TP53, CDK12 and ETS) frequently mutated in prostate cancers and there are hints that these genes could be changing the anti-cancer immune response to help tumors cells hide from detection by our immune system;

2) There are also new molecular kits that allow you to see which specific anti-cancer immune systems are active and which ones are inactive in tumors;

3) By analyzing these four genes in a series of prostate tumors and relating the mutations to changes in activity of the anti-cancer immune system, we will figure out which of the four genes could be causing the anti-cancer immune response to make tumors ‘invisible’ to anti-cancer immune reacting cells.

**BENEFITS:**

1) New information on the molecular signals produced by tumors that allows them to hide from our protective anti-cancer immune system;

2) Other cancers in which the tumors also seem to be invisible to our immune systems may be using the same pathways to avoid detection, and these tumors can be studied in the same way;

3) The genes activated to avoid the immune system in tumors can be used in simple DNA tests to check to see which patients are more likely to respond to immunotherapy.

**SO WHAT?:**

In the future, many patients with life-threatening cancers who have already failed immunotherapy may be given new types of drugs that make their tumors cells more easily detected by our protective anti-cancer responding immune cells.