Gene Therapy: The Basics

What is gene therapy and how does it work?

In the center of every cell in your body is a region called the nucleus. The nucleus contains your DNA (deoxyribose nucleic acid), which is the genetic code you inherited from each of your parents. The DNA is ribbon-like in structure, but normally exists in a condensed form called chromosomes. You have 46 chromosomes, which are in turn comprised of thousands of genes. These genes carry specific instructions that tell cells how to work, control our growth and development, and determine what we look like and how our bodies work. They also play a role in the repair of damaged cells and tissues. Each person has more than 30,000 genes, which are made up of DNA. You have 2 copies of every gene, 1 inherited from your mother and 1 from your father.

So, now that we know what genes are, how can they be used to help fight cancer? If a gene becomes damaged, this damage is called a mutation. This can lead to a gene not functioning properly and a cell growing uncontrollably. This can eventually lead to cancer formation. (Keep in mind that developing a cancer is not quite as simple as this, but probably requires a complex series of multiple mutations.) These mutations may be caused by things like smoking and/or the environment, or they may be inherited. It makes sense that if...
we could repair these mutations, we could potentially stop a cancer from starting. The question is, how do we do this?

Researchers are testing several ways of applying gene therapy to the treatment of cancer:

- **Replace missing or non-functioning genes.** For example, p53 is a gene called a "tumor suppressor gene". Its job is just that: to suppress tumors from forming. Cells that are missing this gene or have a non-functioning copy due to a mutation may be "fixed" by adding functioning copies of p53 to the cell.
- **Oncogenes are mutated genes that are capable of causing either development of a new cancer, or the spread of an existing cancer (metastasis).** By stopping the function of these genes, the cancer and/or its spread of cancer may be stopped.
- **Use the body's own immune system by inserting genes into cancer cells that then trigger the body to attack the cancer cells as foreign invaders.**
- **Insert genes into cancer cells to make them more susceptible to or prevent resistance to chemotherapy, radiation therapy, or hormone therapies.**
- **Create "suicide genes" that can enter cancer cells and cause them to self-destruct.**
- **Cancers require a blood supply to grow and survive, and they form their own blood vessels to accomplish this. Genes can be used to prevent these blood vessels from forming, thus starving the tumor to death (also called antiogenesis).**
- **Use genes to protect healthy cells from the side effects of therapy, allowing higher doses of chemotherapy and radiation to be given.**

**How is gene therapy given?**

You can imagine it would be hard to actually inject these genes into the tiny cells, so a carrier, or a "vector", is used to accomplish this. Typically, viruses are used as the vectors. These viruses are like those that cause the common cold, only they are "deactivated" so that they will not cause the patient to actually get the cold. In some cases, some cells are taken from the patient and the virus is exposed to the cells in the laboratory. The virus with the desired gene attached finds its way into the cells. These cells are allowed to grow in the laboratory, and are then given back to the patient by intravenous (IV) infusion or are injected into a body cavity (i.e. the lung) or a tumor. In other cases, the vector with the attached gene is directly inserted into the patient by intravenous infusion or is injected into a body cavity or a tumor. Gene therapy is still experimental, so the means by which it is given may change as the technology develops.

**What are the side effects of gene therapy?**

Given that gene therapy is so new, we do not know what side effects it may have, particularly long-term side effects that may occur years after receiving this therapy. After initially receiving a type of gene therapy, the patient's immune system may react to the foreign vector, causing fever, severe chills (rigors), drop in blood pressure, nausea, vomiting, and headache. These symptoms typically resolve within 24-48 hours of the...
infusion. Other side effects are dependent upon the type of vector used and how it is given. If the gene is given into a patient's lung, the side effects may affect the lung.

Some side effects are theoretical, meaning that it is feasible that they could happen, yet they have not actually occurred in clinical trials to date. There is a fear that the genes could enter healthy cells, causing damage to them, which could then lead to another disease or another cancer. If genes enter reproductive cells, they could potentially cause damage to sperm or eggs. It is feared that this damage could then be passed on to future generations. At this time, researchers are particularly careful to monitor for these unwanted complications, and perform tests in animal studies before any particular therapy is given to humans.

How do I know if gene therapy is working for me?

At this time, gene therapy on its own is not thought to cure any cancer. It is generally given in conjunction with other therapies with more reliable track records, such as chemotherapy.

That being said, the real answer varies, depending on the type of cancer being treated. Many patients will have radiology studies (CT scans, MRI scans, PET scans) periodically to assess the tumor's status (shrunk, stayed the same, or grown). Some types of tumors can be followed using "tumor markers". Tumor markers are substances that are either produced by the tumor or by the body in response to the tumor, and can be measured by a blood test. If the chemotherapy is working, one would expect the tumor marker to decrease. In some cases, a decrease in a patient's symptoms may be able to signal if the medications are shrinking the tumor or not. Talk with your doctor or nurse about how your response will be measured.