Two Faces of Cancer

By ACSH Staff — March 15, 2012

According to a paper in yesterday's *Journal of Clinical Oncology*, the 5 year survival rate of children with acute lymphoblastic leukemia (the most common form) has continued its upward trajectory, and now stands at 90 percent--fairly amazing considering that it was almost always fatal as recently as the 1960s.

This should not be taken as evidence that the end of cancer is around the corner--it is not. Although there have been a few cancers that are either curable (testicular, for example), preventable (cervical) and more treatable (breast), progress against the disease has, for the most part, been incremental and slow. A recent paper in the *New England Journal of Medicine* offers an peak into why this may be.

When Dr. Marco Gerlinger of the Cancer Research UK London Research Institute and his group examined the genetic makeup of kidney tumors and compared it to that of metastases from the same tumor, they found unexpectedly large differences between the genetic makeup of the original tumor and the cancer that had metastasized. Oncology researchers have long known about mutation of cancer cells, but until this week they didn't appreciate the magnitude of the process. According to Dr. Merlinger, in real life "...a serious flaw in the imagined future of oncology is its underestimation of tumor heterogeneity."

The authors logically concluded that a single needle biopsy of a cancer mass will tell you little or nothing about the genetics of any other masses within the body, and that this would make personalized treatments very difficult. But the implications of this are worse.

The use of specifically targeted cancer therapies (called kinase inhibitors)--new drugs that have been designed to attack a specific growth pathway in the cancer cell--has been the holy grail of oncology research for some time. But much of original hype and promise about this revolutionary approach has not been realized. Ironically, part of the problem is that the very specificity that was desired was too much of a good thing.

Even if you could wave a magic wand and obtain all the genetic information of all cancer cells, there is still not that much you can do about it. The increased specificity of kinase inhibitors limits their damage to non-cancerous cells (fewer toxic side effects), but also decreases their ability to kill mutated cells from the same tumor.

This may explain why it is not uncommon to see impressive responses at the beginning of treatment, with profound tumor shrinkage. However, the mutated cells--which are either part of the original tumor or form later on--will eventually thrive in the space left behind by the original tumor. When the cancer returns it is much less treatable.

This heterogeneity points out one of the big obstacles in oncology research--the lack of a good
animal model. Certain mice are bred to have no immune system. This enables scientists to implant cultured human cancer cells under their skin, and the cells will grow into a tumor.

But the implanted cells are much more homogeneous and more susceptible to attack by the new drug. When treated with the experimental drug, the tumor will often disappear entirely. When applied to real life, things are not so simple. This tumor heterogeneity will be a major barrier to overcome to take this approach to the next level.

It is unlikely that we will see groundbreaking advances in oncology comparable to what happened with other deadly diseases, such as AIDS and hepatitis C, which can now be effectively controlled or cured. Virtually all chemotherapy regimens use one or more drugs that were first used in the 1960s. Reliance on 50 year old drugs as the first line of defense is a good indicator of how difficult the problem really is. There is a long way to go.