

Editorial

**Will therapeutic cloning someday offer hope
for severe mental illness?**

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In a recent abstract in *Scientific American* [1], the primary researchers of therapeutic cloning, or what is otherwise referred to as “cell therapy,” contend that they will one day be capable of providing remedies for diseases of the nervous system as well as for autoimmune disorders. Cures for cardiovascular disease and blood and bone marrow disorders abound in their dreams of future research and development. Once scientists can derive human cells from cloned embryos, the possibilities are enormous, including treatments for spinal cord injuries and even brain disorders.

Let’s take a minute, however, to go back before we move forward. It is important to differentiate between therapeutic cloning and reproductive cloning, which is intended to implant cloned embryos into a female uterus with the goal of gathering a cloned offspring [1]. The concept of therapeutic cloning has drawn considerable ethical debate among scientists and theologians throughout the world, and with good reason. In fact, many believe that ethical constraints are themselves part of the science, but that aside for the moment, the advances in therapeutic cloning and the energetic discourse that accompanies them, leave those of us in the field of mental health with the daunting question: “Does therapeutic cloning raise hope for an eventual cure for refractory mental illness?” The answer, of course, depends on how sophisticated therapeutic cloning becomes and whether or not its future progress includes the critical component of following ethical guidelines.

In the American film, “A Beautiful Mind” [2], Russell Crowe portrays prominent Princeton University scientist John Nash, who received the Nobel Prize for economics for his mathematical principles of game theory. What is particularly unique about Nash’s story is not so much that he is a Nobel Prize winner, but that he achieved this grand award while engaged in a life-long battle with paranoid schizophrenia — one of the most challenging of the mental illnesses. Nash is depicted as suffering from florid delusions and auditory and visual hallucinations. As a result, Nash is treated by psychiatrists who jolt him with high doses of insulin to deliberately induce coma, a

treatment alternative to electroconvulsive therapy popular during the 1950s. The intervention does very little to abate Nash's symptoms, all of which continue to plague him to this day.

Psychopharmacology has served as the predominant treatment for mental illness during the past century, often with marvelous results. Yet, it has only been in the last 25 years that increasing knowledge about the neurobiology of brain behavior and pathogenesis has lit the way to new insights into neural circuitry, cellular pathways, and genetic regulations. We now know that serious mental illness is often the result of complex genetic structures involving many genes and most likely many circuits in the brain. Hence, there are numerous ways that a gene might combine to spawn a particular mental disorder. Unfortunately, what has come to be accepted as classic psychopharmacological treatment for mental illness has probably bypassed many of the gene structures actually responsible for its etiology, modifying only the symptoms and not the true origin of the disease itself [3]. This becomes most apparent in cases in which medication regimes are discontinued and psychiatric symptoms reappear.

Scientists have dabbled in genetics for centuries, but it was the European monk, Mendel, who is credited with conducting the first scientific study of genes. Mendel's experiments, which took shape more than a century ago in an Austrian garden, were the precursors to what we regard today as modern genetics. Mendel, who lived in the mid-1800s, raised many generations of pea plants and carefully observed how traits were inherited. His copious experiments, observations, and critical analysis of the results led to the formulation of the first set of scientific principles, which are often referred to as "Mendel's law of heredity." Mendel could not have conceived of his studies one day leading scientists to experiment with therapeutic cloning.

It was not until recently that several American scientists during a series of experiments prompted human eggs to become fertilized on their own without the use of sperm. These eggs developed through "parthenogenesis" in what is known as "blastocysts" or "hollow spheres of cells," thus coaxing the early embryos to successfully divide. This breakthrough set the pace for therapeutic cloning, which is a process of using genetic material from a patient's own cells to, it is hoped, generate new cells to replace damaged ones.

Genetic scientists and psychiatric researchers largely agree that the majority of mental illness is likely caused by a combination of genes that interact. Studying more basic related phenotypes is most apt to provide a segue to a less complex genetic etiology [3].

With this concept in mind, let us assume that scientific advancement may one day lead to the ability to identify and isolate cells that could serve as replacements for the deficient ones that generate neurotransmitters responsible for certain psychiatric conditions. Thus, the objective would be to remove the mutant genes from cells that are identified as hosts for a particular mental illness and replace them with a cloned (normal) version. The scenario may sound like something out of a Jules Verne novel, yet it may not be so farfetched. We now know that genes can be modified and then successfully returned to an individual's bloodstream. With psychiatric illnesses, the target would be to alter the genetic code of a specific cell disposition without affecting

unrelated cells. This has already been accomplished with a number of medical anomalies such as those related to Severe Combined Immune Deficiencies (SCID), which cause people to be susceptible to massive lethal infections spawned by common diseases [3]. The goal of treatment with such cases is to attempt to modify white blood cells by inserting the missing piece of DNA so that cells can function normally and fight the infection. What makes a similar process with mental illness difficult is that the action may be obscured by the fact that most psychiatric disorders have a more complex mode of inheritance than other medical disorders. Therefore, the task of identifying, locating, and separating specific gene combinations, even with the use of linkage or association studies to narrow the search, is monumental. What is more, gene therapy for mental illness would only deter the genetic code of specific cell structures and not affect transmission to future generations. Finally, we cannot be sure if the cloned cells are even normal.

An additional issue involves deciding which mental illnesses should be treated by such methods. While many would agree that disorders such as refractory depression and severe schizophrenia would be excellent candidates, there are also the personality and anxiety disorders that, even though they cause less subjective distress, still affect millions of people throughout the world. This raises yet another type of ethical concern that will need to be addressed, especially as various mental disorders require prioritization.

Clearly, we still face a barrage of complex hurdles to making a permanent cure for severe mental illness a reality. In the meantime, let us not overlook the bridge between past and future. "Pharmacogenetics," or as it is otherwise known "pharmacogenomics" [4], combines psychopharmacology, a mainstay of treatment, with gene therapy. This may be the answer to improving treatment options now. This burgeoning field involves the study of genes and their role in generating proteins, such as enzymes, and how they function in metabolizing certain pharmaceutical compounds. An initial task may be to determine discrete variations in the function of these key enzymes that may predict how a given patient's metabolism will respond to a particular compound. The isolation of the specific genes that cause particular patients to be slow metabolizers of certain medications, thus increasing their likelihood of experiencing side effects of the drug may be an essential early step to using cell therapy with psychotropic medication. This is especially so for high potency phenothiazines and antimanic compounds, some of which are not always well tolerated by patients. Indeed, once such issues are addressed, this interim step may serve as a bridge to the time when genetic research can effectively identify those groups of genes that render people like John Nash largely prisoners of their diagnosis. This may be one of several steps before we realize therapeutic cloning as a viable alternative.

Therapeutic cloning is definitely on the horizon as an alternative for treating mental illness. It is an exciting prospect even though it remains outside of our immediate reach due to the aforementioned hurdles. In the meantime, however, we must stay engaged in the constant evaluation of ethical concerns, not only as a requirement of some governing agencies but as an essential component of the science itself. This is imperative so that when the time arrives in which therapeutic cloning is an option, we

can embrace it fully and without trepidation.

References

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