

POLICY FORUM

From Mendel to the Human Genome Project

Introduction

Like many of my contemporaries, I looked at the cover of this issue and opened the journal with just a bit of nostalgia, as well as trepidation. For me, genetics brings to mind the ingenious monk Gregor Johann Mendel and his experiments of crossbreeding hybrid peas in his garden. Genetics also evokes memories of an inspirational teacher who let his students catch hovering *Drosophila melanogaster* and then assigned us the task of counting the number of white-eyed and red-eyed fruit flies in each generation to demonstrate single-gene inheritance. In college and medical school, I began to appreciate the strange beauty of the double helix and the mechanisms through which DNA directs the inner workings of each cell. When James Watson and Francis Crick untangled the helix into double strands of well-strung pearls with 4 variations—adenine, cytosine, guanine, and thymine—researchers thought they had unloosened the Gordian knot of all time.

But not so fast. The double helix could be stained, colored, unwound, and isolated. First we sorted DNA into pairs of chromosomes, and then we began to see how chromosomes could be stuck together or pulled apart, resulting in deletions or duplications of entire chromosomes. In the twisting and spinning wild dance of replication, those ACGT base pairs could, and would, mix it up even more. Then our stains and microscopes got even better. Francis Collins led the Human Genome Project in its attempt to uncoil, unwind, and reveal the sequence of all of the genes packed into our chromosomes. This work began an ongoing investigation to determine what pieces, fragments, and sequences of which base pairs influence what traits, and when.

This issue of the NCMJ takes us further and wrangles our twisted genome to show that we can have base sequences in the right order yet with different expressions that can mean, literally, a difference of life or death. As we continue to explore the human genome, we often do not even know what we have discovered.

Genetics is not as simple as Gregor Mendel suggested, as we were bound to discover. Exposure, expression, and probability add to the crazy beauty—and mystery—of the genomic dance, one in which 4 partners create all the diversity of the world. NCMJ

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