

## Editorial

### **The Genomic Era: “It’s Just the Way I Am” Gives Way to “Look At What I Might Become!”**

If I had to say what’s the most persistent, important question running through a doctor’s mind as he or she listens to a patient, I’d say it’s simply this: Why? Why is the patient having this symptom? What illness might it represent? How accurately the physician resolves the question and how effectively he or she can persuade the patient to collaborate in a reasonable plan to restore or preserve health will determine how well that patient ultimately fares.

For several years, I’ve been asked to give the opening lecture for the Physical Diagnosis course we offer at Columbia University to second-year medical school students who are about to have their first contact with patients. It’s my job to help prepare them for their initial look at an actual sick person and to preview at least some of the unexpected challenges they face. As a very bright psychoanalyst once told me, “The transition from the drawing room to the examining room can be a very difficult one.” I am always reminded of that response as I look out at the sea of 150 young faces in the amphitheatre, just at the threshold of their medical lives and usually too young to have experienced any of the pain they will be expected to understand and address. For the most part, they are completely unaware of how complex the demands of their vocation will prove to be.

The physician–teacher has several important mandates. The first is to help the student develop a combination of relevant information, empathy, and kindness that makes the encounter for the patient as painless and useful as possible. Just as important, the student must be prepared for the things the suffering sick person will expect: some are rational and possible; others, unreasonable and completely beyond any doctor’s power to provide. Whether or not they verbalize it, most patients want freedom from aging and decay. They hope that all their pain, both physical and psychic, will be relieved promptly and with a minimum of effort and risk on their part, and in the process, they hope to be loved or at least genuinely liked by their doctors. All patients fervently anticipate that those doctors will have magical powers to restore them to health and, ultimately, to permanently postpone the moment of their death. Obviously then, one of the most compelling challenges is to manage the sick person’s expectations and to help him or her deal with the fact that as powerful as we doctors seem to have become (and as ardently as the patient may wish it), immortality is still not within our grasp to bestow on our patients.

Clinicians who are embedded in an academic medical center have an advantage in training young doctors: we are constantly exposed to a flood of new scientific information that helps explain what patients are experiencing and what will happen to them. This has always been the case, but I think that we are in a new era of medicine based on what is arguably the greatest of all our human achievements—the sequencing and analysis of the human genome. It certainly ranks up there with our other most spectacular accomplishments, such as the invention of the printing press or the discovery that the world is round and revolves around the sun. Our work with the genome is defining not only what we are, but why we are that way...and how we can modify and change it. Along with the patients we serve, the boldest of the genomic scientists dream of prolonging the human life span indefinitely, of banishing the specter of old age and its myriad attendant ills, and of vanquishing disease and infirmity. As doctors, we dream that, in the foreseeable future, we will be able to reach into our patients’ genetic apparatus and with a broad understanding of all the factors that control its expression, eliminate what will or has made them ill, flawed, and mortal. Every day, incredible things are happening. Scientists like George Church have made it possible to take the simple building blocks of life and fashion entirely new organisms, themselves capable of reproduction, that are designed to accomplish novel and very specific tasks that will be of

unique service to mankind. I discussed this topic with a colleague recently and asked him if he thought our new, bold experiments were interfering with evolution. He answered that the expanding competence of humans to change the very nature of created life *was part of evolution*.

For the time being, although it seems impossible to overestimate what we will achieve in the next decades, our knowledge of how genes work and how their expression is controlled and modified is enough to keep us more than occupied, and gratified and amazed as well. In the current issue of the *Proceedings of the National Academy of Sciences*, Way et al<sup>1</sup> reviewed data showing why humans feel physical pain under the stress of what the authors call “broken social ties.” It appears that the neurologic infrastructure in the brain that produces our perception of and response to either physical or psychic pain is similar, and in some respects identical.

Reading this, I was reminded of a woman who told me that when her husband died, she felt as though her skin were literally on fire; an equally useful observation from the same report is that individuals may experience very different degrees of the intensity with which they experience psychic or physical pain because of a naturally occurring variation in the human *OPRM1* gene that controls the expression of the brain’s  $\mu$ -opioid receptor (MOR). A low level of receptor predicts an increased sensitivity to physical pain (and a concomitant need for higher doses of morphine to treat such pain) as well as to the pain of social rejection or abandonment. A complementary study by Barr et al<sup>2</sup> found that the development of attachment for a caregiver is mediated in baby primates (including humans) by functional differences in the MOR gene that regulate the intensity with which they attach to their mothers and, conversely, how joyously comforted they are when reunited with their mothers after separation. Perhaps we now can begin to understand the genesis of shyness, of the difficulty some have in living alone, of one person’s bitter complaints of pain in response to stimuli that are shrugged off by others—even the inconsolable anguish of an individual who loses a beloved other and cannot seem to recover. While it is true that phenotype depends on the intricate, complex, and only partially understood dance between genes, experience, and hormones, it is clear that to a great and increasingly predictable extent, our genetic equipment determines what we are. Indeed, every genomic scientist of note predicts that we will be able to develop new ways of modifying behavior and of preventing disease or disability through genetic manipulation.

At this moment in time, though, at the beginning of the 2009 school year, all I was able to tell my nascent doctors is that their patients’ individual genome has a profound impact on how they behave. Certainly, it explains the wide variations in human sensitivity to emotional and physical pain. Treatment for each person’s suffering, therefore, has to be individualized, and each person’s response to that suffering accepted as a condition of what he or she is, and not necessarily what we would like it to be.

There is obvious truth in the statement, “It’s just the way I am.” But, given the strides we are making, none of us believe it necessarily follows that what our patients are, they will always and inevitably be. At the very least, we hope to leave them in better health and, to a real extent, living more competent, happier, and longer lives.

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## REFERENCES

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