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Claremont McKenna College Opening Convocation 2010

## **Mapping the CMC Genome**

*Gretchen Edwalds-Gilbert, Associate Professor of Biology*

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Thank you Dean Hess for the introduction and for inviting me to deliver the convocation address. I would like to extend my welcome this morning to President Gann, members of the Board of Trustees, my fellow faculty, staff, and students, especially those of you beginning your college studies today. I also want to join in congratulating those who have been honored for 25 or more years of service.

This year I reach the 10 year mark. Ten years ago I began my position as a molecular biologist in the Joint Science Department. Ten years ago another and much more significant event took place: the mapping of the human genome. That achievement was not only the culmination in our knowledge of human biology, it was the beginning of new and important paths in biological research, research that will enable us to further understand how the human body functions, and how to design better ways to combat human disease. To help commemorate this milestone in science, I have entitled my talk this morning, "Mapping the CMC Genome."

As in any academic enterprise, I begin with a series of questions. What is a genome; how does it function within the human body, and in what sense does CMC have a genome? If I were in the classroom rather than McKenna Auditorium, I would first want you, my students, to think about these questions and offer some preliminary answers, answers based on information at hand that we could test and either accept or reject, the basis of the scientific method. CMC thankfully does not have classes this large, so let me offer a few observations of my own. First, a genome is the complete DNA sequence of an organism. DNA is constructed of four nucleotides, represented by the four letters G A T C. The nucleotides provide the building blocks for life in the cell or organism and are housed in The Nucleated Cell, or TNC, which I hasten to add serves a very different function than the TNC that functions as a building block of life at CMC. This sequence of nucleotides varies in size and can be as small as the 5 million base pairs of DNA in single cell bacterium, or the 3 billion base pairs arranged in 23 pairs of chromosomes in humans. If you were to write out the entire human genome in a book, it would occupy approximately 600,000 pages. Next to the human genome, *Moby Dick* looks like a short story.

Our understanding of the human genome, like all scientific knowledge, is built on previous discoveries starting with the initial understanding of DNA in the 1870s to the discovery of the structure of DNA, the famous double helix identified in the 1950s by Watson, Crick, and, often ignored but no less vital, Rosalind Franklin. With this knowledge, scientists could begin the daunting challenge of mapping the 3 billion base pairs of DNA in the human genome. A preliminary step came with the mapping of the yeast genome. The yeast genome contains a mere 12 million base pairs, but if you come to work in my lab, where yeast is the model system, you will come to recognize the amazing power of yeast. These studies showed not only that it was indeed possible to map the entire genome of an organism, but also demonstrated the remarkable similarity in genomic content between yeast and humans. Therefore, the next time you drink that beer, think about it, you are drinking a bit of yourself, so show some respect.

Why are scientists interested in mapping the human genome? And why is it valuable to do so? The human genome project, which had as its goal the sequencing of the entire human genome, began in 1990, and was undertaken by two competing groups, one funded by the government and a second by a private company. Both projects promised not only a complete map of the human genome, an important advance in our understanding of human life and its evolutionary history, but also information that would enable scientists to treat human disease by targeting specific genes and developing personalized medicine -physicians could determine what treatments would or would not work for an individual with a specific genetic makeup. The past decade has seen significant advancements in this area. We now use gene sequencing information to determine disease susceptibility and to develop gene therapy for diseases such as cystic fibrosis and certain cancers.

My current research applies the information gained through genome mapping and seeks to understand the role genes play in protecting us against environmental toxins. In one project, my students and I employ comparative genomics, trying to understand which genes respond to environmental toxins such as food preservatives or the plastics additive bis-phenol A, better known to water bottle aficionados as BPA. Working with the library created by the yeast genome project, we can remove, or knock out, one gene at a time from the genome. We then expose the intact yeast, our control, and the modified yeast to various chemicals to determine exactly which genes regulate a response to the toxins. With this information we can then examine the related human genes and their association with susceptibility to toxins. My lab is working on this project with my Joint Science colleague Professor Irene Tang, who studies an evolutionarily distant and more complex relative of budding yeast, and with Professor Katie Purvis-Roberts, an environmental chemist. One of the advantages of working in Claremont is that we have the opportunity to collaborate with colleagues at Harvey Mudd and Pomona on the computational and functional genomics, making this a truly Five College project. Together, we are trying to decipher the genetic networks required for response to environmental toxins, if they are the same in yeast, my model and *S-pombe*, the model studied by Professor Tang, and whether the same processes exist in human cells.

Through the human genome project we have learned that humans and fruit flies are almost identical when it comes to the number of protein encoding genes, the genes that carry out cell function and therefore expressing phenotype. So here is a question: how is it that the same genes, possessed by both humans and flies, can produce such vastly different organisms? The answer is RNA, the true leader of nucleic acids. What makes us different from flies is that when the human cell makes the pre-messenger RNA during transcription it can make a wider variety of mature messenger RNAs through alternative splicing. Or to put it differently, our RNA functions differently than the RNA in flies. One pre-messenger RNA can lead to many different mature messenger RNAs which in turn lead to many different proteins, all from a single gene, which has the result of producing a much more complex organism, such as a human. We have also learned of other players in the cell that contribute to developing a complex organism, but you will have to take biology to learn more about those.

At the beginning of the human genome project many scientists harbored great anticipation that this new information would provide us with a complete map of how the human body functions. We would know, once and for all, what makes a human, human. As in much of science, the

results proved different than the hypothesis. We now recognize that the DNA sequence does not tell us all the information we need to understand about how a cell works, much less how an entire person functions. DNA sequence tells us what genes an organism has, but not the genes it uses. In other words, just having a map does not get us to the final destination. Those of you who have studied biology will recognize this characteristic as an emergent property commonly seen in biology. An emergent property means that the whole is more than the sum of its parts, such as a cell being more complex than just a combination of individual molecules. Another important finding from the human genome project is that each human genome is different, and that difference matters. People vary not only in the numbers of genes they have, but more importantly how they use, or express, those genes. Regulating what genes are expressed (or not expressed) is more complicated than previously recognized, and finding the sequence is just a first step. Ultimately, it all comes down to how genes, the basic building blocks of the human organism, are regulated. Finally, it is important to note that while RNA and proteins play a considerable role in cell regulation, other factors are involved in human function. One might say that DNA is not destiny. The choices we make as human beings, even with our genomic structures, contribute to the regulatory process.

Human institutions, unlike human bodies, do not have a genome, at least not in the way a genome can be studied in the lab. We cannot extract their DNA, sequence it, clone it, or express it. Nonetheless, institutions, such as colleges, are regulated in ways not unlike the human genome. Institutions do not have nuclei, but they have leaders, some of whom are in the making. Institutions do not have RNA or proteins, but they do have missions and mottos, rules and customs that regulate the life of the community. How then, might we ask in this heuristic exercise, can we map the CMC genome?

CMC possesses numerous mechanisms that regulate what we, as a community, do and who we are. Perhaps nothing defines us more than the mission of the college. CMC describes its mission as a college that seeks “to educate its students for thoughtful and productive lives and responsible leadership in business, government, and the professions.” According to this statement, we are an academic community that emphasizes leadership in economics, government, and international relations. Like a gene and its phenotype, we can observe how the mission is expressed through a top ranked faculty in these areas, including those appearing on Fox Business Report; through internships that allow students to apply the knowledge you gain in the classroom to real world settings, institutes where you can work collaboratively with faculty in research, and through career services and professional networks that afford amazing opportunities in business, banking, government, law, and foreign service for you to pursue after graduation.

Or take the example of the college’s motto (Say it with me): *Crescit cum commercio civitas*. Which means what? Civilization prospers with commerce. These four short words capture CMC as an institution that emphasizes commerce, economics, and finance; a focus that certainly brought many of you to this college. The college’s mission and motto, the RNA and proteins in the CMC organism if you will, along with a host of customs and traditions, regulate the college’s structure and its curriculum.

As the human genome project has taught us, however, our DNA is not destiny, and human action, along with biological mechanisms, produce the human beings we are. So too, the regulating mechanisms of the CMC genome shape who each of you is, but do not control you. To speak of “the professions” reminds me of the Simpsons episode in which Apu responds to Ned Flanders who describes the world’s religions as Christians, Jews, and miscellaneous. After all, the Hindu notes, there are one billion of us. “The professions” is more than a miscellaneous category, and includes, if I might make a plug here, the important contributions made by scientists. And certainly civilization prospers with more than just commerce, but requires a diversity of personal and professional interests. *Crescit cum commercio et historia et arte et lingua et philosophia et religione civitas*. How you engage the CMC genome, your choice of classes, the internships you experience, and the majors you study will contribute to the CMC student you become. It is up to each of you to determine how best to make use of the amazing array of resources, the CMC genome, available to you, and in so doing create a meaningful college experience that will guide and inform you not only during the next four years but for the rest of your lives. Good luck!