Experimental Man

Outtake from **Environment: "Do my genes protect me?"**

This section was mostly edited out of the final draft of the book. See pages 161-162 in the book.

Carolyn Mattingly ran one more test for me. Because genes and SNPs do not operate in isolation in our bodies, scientists are beginning to develop software and computing power to track a change caused by a mutation – or a chemical – in one gene with what happens to other genes that interact in pathways and systems that regulate, say, inflammation or metabolism. For instance, if mercury or PCBs cause a gene to ramp up or down its activity, this can affect its ability to activate or otherwise impact the next gene, which can cause an entire pathway to malfunction. Imagine a line of cars on a long bridge moving at a steady, if frustrating 30 miles per hour, when a driver with allergies suddenly has to sneeze. He tries not to, but it cannot be helped: Achew! The sneeze causes him to slow down ever so slightly, which affects all of the cars behind him. The delay ripples down the line, causing a cascade of cars to reach the other side of the bridge later than they would have without the sneeze. Something like this happens in genetic pathways when one gene is impacted by, say, mercury.

Connections between environmental toxins and pathways is in most cases very preliminary, but Mattingly was nice enough to send me two diagram that

look like the electrical schematics on the back of my fuse box in my garage. The first chart shows a field of about 35 genes that are influenced by my 40 top chemicals. Mattingly created the chart using a commercial software package that show how these genes interact with one another – and how impacting one of them can affect others. Take the gene called CFB, which is involved in immunological responses – and responds to mercury exposure by decreasing its activity. According to the diagram, this alteration in CFB expression might cause other genes “downstream” to be altered, too, causing complications in critical pathways and possibly triggering a disease response.

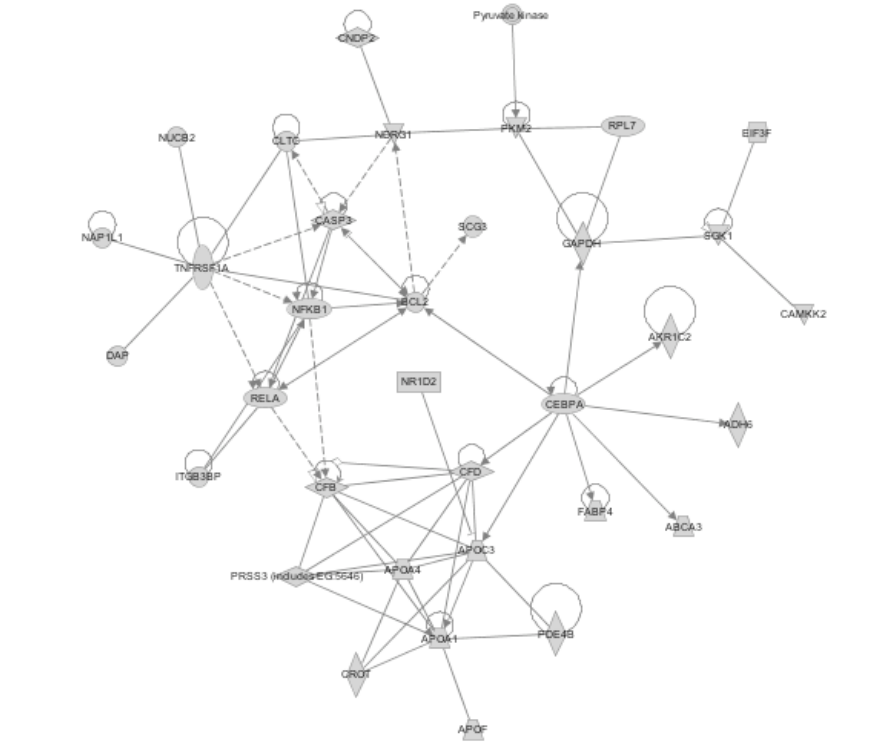

Chart of the interactions of 35 genes impacted by 40 chemicals inside the author.

The second chart details the interactions of genes involved in my respiratory system. This system includes over 30 genes that have something to

do with diseases ranging from asthma and migraines to heart disease. In this system, I've singled out two genes that are impacted by environmental toxins inside me. For one gene, I have a high-risk variant, for the other, the normal variation.

For the first gene, ADRB2, my variant in very early and sketchy studies suggest a slightly elevated risk of migraines, asthma and perhaps heart disease. At the same time, exposure to certain heavy metals such as cobalt and copper also cause this gene's activity to increase. The combination of these two factors zapping this gene is not known, but it's likely to cause changes up and down the pathways that ADRB2 is a part of.

Gene-Chemical Interaction:						
Respiratory Disease Pathway						
Chemical	**Reaction**	**Gene**	**SNP**	**Risk Variant**	**DED Result**	**Disease**
Metals (Colbalt, Copper, Zinc)	⬆ expression	ADRB2	rs1042713	A	AG	Migraines, Asthma, heart disease
Metals (mercury)	⬇ expression	F5	rs6025	C	CC	Thrombosis; interferes with clotting/increases risk for stroke

Mercury and other metals have been shown to turn down the activity of the second gene, called F5 – which controls part of the process of blood clotting. Reducing the expression of this gene can interfere with the process of clotting, a condition called thrombosis (ck this). Having a certain SNP mutation of the F5 gene can also cause thrombosis, and increases the risk of stroke. For this gene, I have the normal, or lower-risk variant, though if I had the higher risk version,

having metals on board might have amplified the deleterious affect. In other words, the high-risk variant plus mercury would not only be bad for a person carrying this gene, F5, but it might also cause changes up and down the pathways of this entire system.

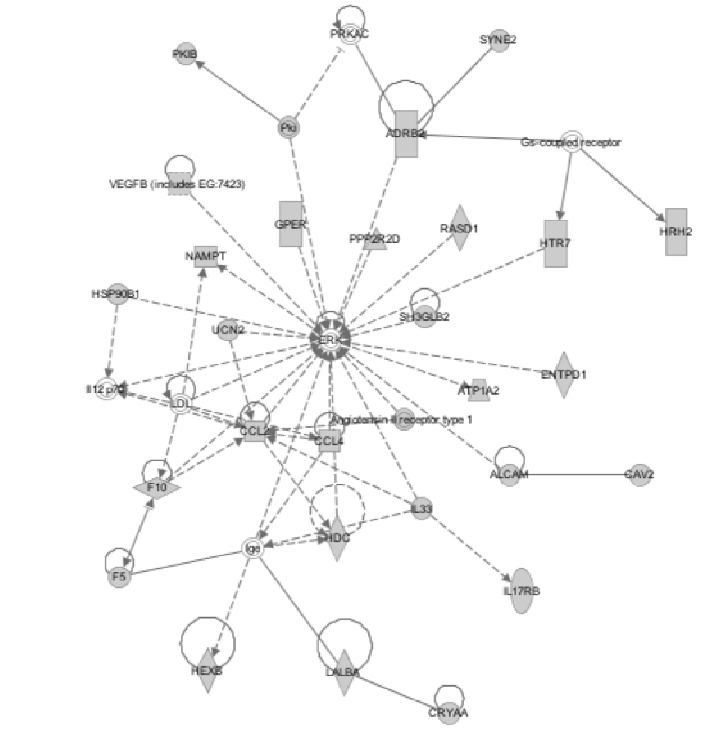

Chart of a pathway of genes in the respiratory system.

As the afternoon waned, I said good-bye to Carolyn Mattingly and headed back out into a blast of freezing air, making a dash in the snow to my car while my head spun with what she had been explaining to me. Without question the charts linking interactions with genes, chemicals and disease pathways will be a crucial part of the future of personalized medicine – though clearly it is far too early to be of much use to individuals. Yet even in its crude form I could tell that it

contained powerful information about the impact of chemicals on the delicate and dynamic balance of forces inside our bodies. Like the man in the car on the bridge who couldn’t help sneezing, I felt as I headed away from Acadia and the lab at the ends of the earth like I had just learned what could happen if I slowed down (or sped up) the actions of my genes even slightly: how it would impact entire systems inside me. With more snow threatening and the sky turning dark and pregnant with moisture, I felt something about my body that I never had before: fragile.