



### // MISSED THE LAST ISSUE?

All stories from *Proto*, Summer 2008, are available at [protomag.com](http://protomag.com).

## Surveying the Flu

In “Flu Central” (Summer 2008), the infographic charts the progress scientists have made tracking influenza’s evolution, as the virus travels around the world from its birthplace in Asia. Also important in predicting which flu strains will emerge—and hence in devising vaccines against them—are the strains’ genomes. Two proteins (antigens) on the virus’s coat have been the main focus of surveillance efforts. But our laboratory at the University of Pittsburgh School of Medicine has found that using whole genome data, in which all gene segments are sequenced and analyzed from populations of viruses, leads to a better understanding of the virus’s evolutionary dynamics, allowing us to identify new markers of the virus’s evolution over time and space.

Within a host infected with viruses belonging to different subtypes or strains, reassortment of the gene segments can occur, leading to the creation of novel viruses. In fact, reassortment is a major driver of the virus’s seasonal evolution and the potential source of pandemic strains. Whole genome analysis clearly demonstrates that even minor viral lineages can contribute genetic variation resulting in significant strains. For example, the flu vaccine’s limited effectiveness during the 2003–2004 season can be blamed on reassortment between a minor lineage variant co-circulating with a major variant (the latter having been chosen as the vaccine strain). The advantage of sequenced-base sampling is that all co-circulating strains can be identified even before they become dominant.

The Influenza Genome Sequencing Project, begun in 2004 by the National Institute of Allergy and Infectious Diseases, has so far sequenced more than 3,200 complete genomes of influenza A and B. The data has led to a better understanding of

viral evolution and reinvigorated surveillance efforts.

**Elodie Ghedin** // Division of Infectious Diseases, Department of Medicine, University of Pittsburgh School of Medicine

## The Body Inflamed

I read with interest “Always On” (Summer 2008), which describes the link between chronic low-level inflammation and many diseases, including cancer. As early as the 1800s, scientists suspected a link between cancer and inflammation, yet that link has gone unappreciated until recent years.

The triggers of chronic inflammation that increase cancer risk include microbial infections (such as *H. pylori* for gastric cancer and mucosal lymphoma), autoimmune diseases (inflammatory bowel disease for colon cancer) and inflammatory conditions of uncertain origin (prostatitis for prostate cancer). But the inflammation-cancer connection is not restricted to a subset of tumors; rather, an inflammatory component is present in most tumor tissues.

The Istituto Clinico Humanitas in Milan and other institutions have shed light on two pathways that link inflammation and cancer, as reported in the journal *Nature* this year. In one, activation of certain oncogenes drives the expression of inflammation-related genetic programs. In the other, inflammatory conditions such as those mentioned above promote cancer development.

Current efforts are aimed at translating progress in understanding the fundamental mechanisms of cancer-related inflammation to the bedside; results so far are encouraging.

**Alberto Mantovani** // Research Laboratories in Immunology and Inflammation, Istituto Clinico Humanitas, Milan

### → WHAT’S YOUR TAKE?

Write to [protoeditor@mgh.harvard.edu](mailto:protoeditor@mgh.harvard.edu) to comment on a story—or offer suggestions for future topics.