CAD (p<0.05). In a pooled analysis, the odds ratio per copy of the risk allele was 1.29 (95% CI, 1.22 to 1.37; p=0.0001). An autosomal-additive mode of inheritance best explained the underlying association [Schunkert H et al. *Circulation* 2008].

Two sequence variants on chromosome 4q25 that are adjacent to PITX2 (which has a critical function in left-right asymmetry of the heart) confer risk of AF. The association is inversely related to age. About 35% of individuals of European descent have at least one of the variants, and the risk of AF increases by 1.72 and 1.39 per copy [Gudbjartsson DF et al. *Nature* 2007]. Nine validated SNP variants on chromosome 1p13.3 have been associated with modulation in levels of LDL or HDL cholesterol, and the incorporation of them into a genotype score improved clinical risk reclassification in a cardiovascular cohort when added to standard clinical factors [Kathiresan S et al. *N Engl J Med* 2008; Sandhu MS et al. *Lancet* 2008].

Dr. Topol believes that this 'treasure trove' of genetically linked lipoprotein biology may lead to novel therapeutic interventions if a few caveats can be overcome. He cautioned that we are still working with incomplete coverage of the genome and that structural variants are complex and much larger than initially hypothesized [Korbel JO et al. *Science* 2007]. Structural variation of the genome involves kilobase- to megabase-sized deletions, duplications, insertions, inversions, and complex combinations of rearrangements. Epigenomics (processes that regulate how and when genes change) and epistasis (when the action of one gene is modified by one or more genes) are not completely understood and may impact the disease process in unpredictable ways. In many cases, the observed effects actually result from multiple SNPs that act in concert within a gene, and thus analysis of a few variants per gene is not likely to be sufficient to identify potential functional effects.

Nonetheless, the 'age of the genome' is truly upon us, with private companies beginning to offer genome "scans" that claim to have the ability to predict the risk of many types of diseases. Next to come will be a consumer genome movement and genetic home testing kits. The physician needs to be prepared for the day when patients begin showing up in their offices with individual SNP profiles asking for interpretation of their health risk factors. Dr. Topol's final comment was presented in a slide titled "The Resequencing Imperative"—"..when genome-wide resequencing is practical and affordable, it will be increasingly difficult for the genomic basis of health and disease to be left undetected."

Cardiac Infections

The first symposium developed jointly by the American College of Cardiology and the Brazilian Society of Cardiology, provided an overview of infectious diseases of the heart. The session featured an important review of viral and parasitic infections of the heart and the role of infection in myocarditis, pericarditis, and coronary artery disease CAD.

In her presentation, Dr. Maria de Lourdes Higuchi, MD, PhD, The Heart Institute, Sao Paulo, Brazil focused on *Chlamydia pneumonia* (CP) and *Mycoplasma pneumoniae* (MP), 2 microorganisms that have been implicated in bacterial infection and inflammatory conditions of the heart and pericardium. MP requires cholesterol for survival, and because vulnerable atheromas are rich in cholesterol, they may provide a favorable environment for MP growth. Studies have confirmed that MP is found primarily in the lipid core of ruptured thrombosed plaques. In addition, mycoplasma may increase the virulence of other infectious agents; for example, Dr. Higuchi noted that research has demonstrated a symbiotic relationship between *Mycoplasma hominis* and *Trichomonas vaginalis* [Dessi et al. *Infect Immun* 2005]. "Species interaction forms more stable and productive colonies," she said. The result is more resistant chronic infections.

In CAD, coinfection with MP and CP may represent an important contributor to plaque inflammation, instability, and rupture, because greater amounts of MP and CP have been strongly correlated with histologic signs of increased plaque vulnerability. In other studies, CAD or myocardial infarction (MI) has been found to be more prevalent among individuals who are seropositive for both MP and CP, and elevated levels of serum MP and CP antibodies have been found in association with acute MI.

Dr. Higuchi also noted that small amounts of MP and CP have been found in some vessels without atherosclerotic plaque, suggesting that another factor may contribute to the proliferation of these microorganisms. Her research has shown that vulnerable plaques also contain archaea, the most primitive microorganisms [*Clinics* 2006]. The powerful antioxidative enzymes of archaea may enable them to enhance the survival of aerobic microorganisms such as MP and CP and to participate in the pathogenesis of plaque vulnerability, said Dr. Higuchi. She added that effective treatment will require targeting the fundamental pathways that maintain the symbiotic state of the microorganisms.