Center for Discovery & Innovation
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Dr. Tycko, M.D., Ph.D.

Dr. Tycko joined CDI from Columbia University. Research by Dr. Tycko's group combines genetics and epigenetics. Their work, which has been continuously NIH-funded for nearly three decades and includes a web of collaborations with scientists from other medical centers, has been published in many top-tier scientific journals. Novel methods and analytical approaches developed in his lab have uncovered fundamental mechanisms that control gene expression and are now seeing practical applications across a wide range of human diseases, including autoimmune disorders, brain diseases, and cancers.

While in some cases single gene mutations can have strong effects on disease risk (such as BRCA1 and BRCA2 gene mutations in breast cancer), for most common human diseases the situation is more complex, with contributions from many genetic variants adding up in each person to confer the disease risk. In the past 20 years, many expensive publicly funded genome-wide association studies (GWAS) have pointed to genes and chromosomal regions that each confer a small incremental risk of disease. We are now in a "post-GWAS" era, in which one of the most important but technically difficult goals is to capitalize on this investment to determine not only the repertoire of culpable genes for each disease, but also the precise DNA sequence changes that lead to problems with the expression of these genes, and hence the disease risk. This knowledge could then be used to design genetic screening panels that could save lives and billions of dollars in healthcare costs by targeted testing and screening procedures, both for the patient and for his or her family members.

Dr. Tycko's research has focused on epigenetics, which is the study of changes in the DNA and its packaging in the cell nucleus that can affect gene expression without alterations of the classical genetic code. "Epi" means "on top of", and epigenetic marks are biochemical modifications that cells place on top of their DNA sequences, without changing the sequences. One of the best-studied and useful epigenetic marks is DNA methylation. To help meet the post-GWAS challenge, the Tycko lab employs extensive whole-genome methylation sequencing (methyl-seq) to find small chromosomal regions that show asymmetry in methylation patterns between the two alleles, that is, between the chromosome that was inherited from the mother and the one that was inherited from the father. Building on their initial proof-of-principal study that they published in Nature Genetics in 2008 and followed up with additional publications, they are now overlapping their large methyl-seq datasets with GWAS, to home in on the exact repertoire of DNA sequence changes that add up to produce disease risk. This work, which crucially involves statistical and bioinformatics expertise of Drs. Catherine Do and Emmanuel Dumont in the Tycko lab, is now being pushed forward as a collaborative team effort with other scientists at the HMH-CDI and elsewhere, and with clinicians at HUMC. It is benefiting crucially from the new infrastructure for genome sequencing and computational biology in the CDI – areas that will continue to expand through investments and strategic recruitments in the near future.