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ABSTRACTS

HGM2008 plenary abstracts: landscape of genomic variation

004: Human genome structural variation, disease and evolution

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Structural variation of the genome is an important aspect in our understanding of human disease and evolution. I will focus on the genome-wide discovery, analysis and distribution of copy-number and structural variants within the "normal" human population with a particular emphasis on resolving these events at the single basepair level. I will summarize data from a project to catalogue all structural variation from the genomes of normal individuals using a clone-based sequence approach. I will present data showing how common structural polymorphisms may predispose to genetic disease and how historical hotspots of variation can be used to identify previously undescribed microdeletion and microduplication syndromes associated with various forms of pediatric disease including mental retardation, epilepsy, diabetes and renal disease. I will present these differences in the context of the evolution of our genome and provide examples of how these regions simultaneously predispose to disease as well as being potentially adaptive during human genome evolution. The challenges and importance of resolving historical and contemporary structural variation will be discussed.

005: Extensive structural variation in the human genome revealed by paired end sequencing

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Structural variation of the genome involves kilobase- to megabase-sized deletions, duplications, insertions, inversions, and complex combinations of rearrangements. We introduce high-throughput and massive paired-end mapping (PEM), a large-scale genome-sequencing method to identify structural variants (SVs) approximately 3 kilobases (kb) or larger that combines the rescue and capture of paired ends of 3-kb fragments, massive 454 sequencing, and a computational approach to map DNA reads onto a reference genome. PEM was used to map SVs in an African and in a putatively European individual and identified shared and divergent SVs relative to the reference genome. Overall, we fine-mapped more than 1,000 SVs and documented that the number of SVs among humans is much larger than initially hypothesized; many of the SVs potentially affect gene function. The breakpoint junction sequences of more than 200 SVs were determined with a novel pooling strategy and computational analysis and revealed that SVs arise by homologous and nonhomologous recombination and by transposition events. Our analysis provides insights into the mechanisms of SV formation in humans.