

New insights into the mechanisms of human disease

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Recent advances in genomic technologies are opening up new vistas in our approaches to understanding not only Mendelian single-gene anomalies, but also more common later onset diseases. The growing capacity to dissect genomic information on a large scale is revealing new mechanisms for perturbing "normal" function at every stage of life. Relatively conventional genomic analysis has uncovered unexpected features of genomic organisation including the presence of large tracts of low copy number repeats which may be associated with dynamic copy-number variation, some associated with disease. Such variation can now be routinely identified using genomic arrays. Genome analysis has also uncovered the presence of several types of non-coding RNAs whose function is now being deciphered and, in some cases being associated with abnormalities. Evolutionary sequence comparisons have revealed the prevalence of highly conserved non-coding regions of DNA and in many instances regulatory function has been assigned to these. The ability to study single nucleotide polymorphisms on a large scale in large disease cohorts and normal controls is fueling the era of genome-wide association studies, where disease-predisposing genes are uncovered and provide growing understanding of normal biology as well as deviations from the norm. About half the common disease-associated variants lie within the regulatory regions of the genome, making functional identification and validation a new and exciting challenge. Galloping increases in sequencing capacity are opening the door to whole-genome sequencing of many individuals. The capacity for generating vast quantities of sequence data is producing a strong demand for the development of novel bioinformatic approaches to data analysis. The possibility of sequencing many esoteric model organisms provides exciting insight and new tools for biology and promise for the development of therapeutic approaches.