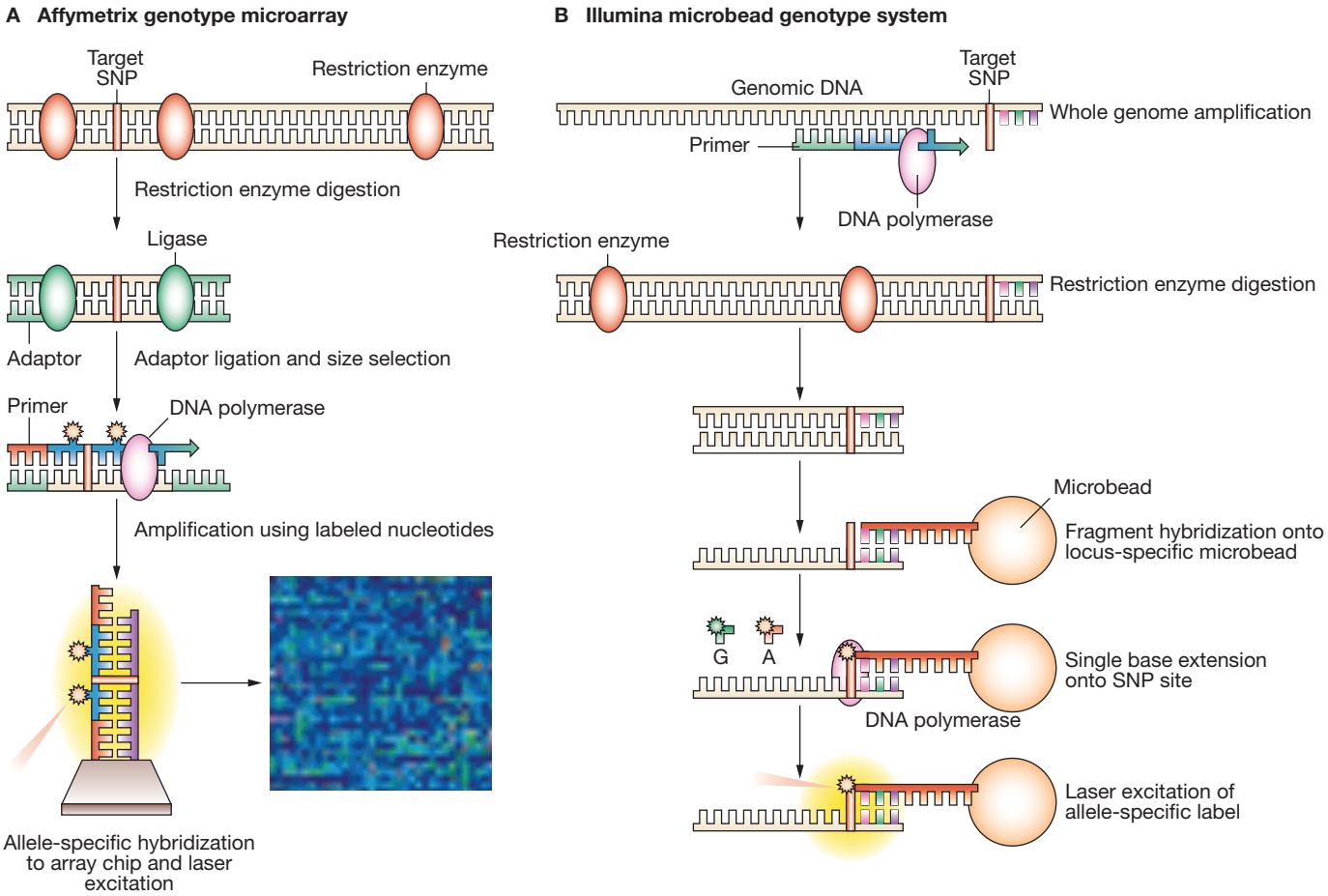

Figure 2 Two ultra-high-throughput single nucleotide polymorphism genotyping platforms for use in genome-wide association analyses. (**A**) SNP genotyping using Affymetrix (Santa Clara, CA) high-density oligonucleotide microarrays. Genomic DNA samples are digested into fragments of random sizes using a restriction enzyme. Adaptors are then ligated to the fragment ends to create universal priming sites for PCR amplification. Fragments of sizes 250–1,000 bp are amplified, fluorescently labeled and hybridized to the array. The arrays are scanned and SNP genotypes are determined using specialized software following laser detection. (**B**) SNP genotyping using Illumina bead arrays (San Diego, CA). Genomic DNA samples are subjected to genome-wide amplification and the amplified DNA is then fragmented by enzyme digestion. Fragments are hybridized to SNP-specific bead chips, each of which carries two probes that enable simultaneous genotyping of both SNP alleles and that anneal with template DNA at a site one base before the SNP. The annealed DNA is now extended by a single labeled base, depending on the genotype at the SNP. The extended samples are stained to amplify the signal and allow detection of the incorporated base by laser excitation, and genotypes are determined using an array reader and specialized computational software. Abbreviations: PCR, polymerase chain reaction; SNP, single nucleotide polymorphism.

paving the way for the routine sequencing of whole genomes, a capability that will almost certainly transform the disease gene discovery field and the pace and clinical impact of all genomic sciences.

MICROARRAY-BASED GENE EXPRESSION PROFILING

The effective translation of genome sequence data into the biological understanding of disease necessitates tools that enable not only genes, but also their products, to be evaluated on a global genome scale. One particularly powerful approach to such 'functional' genomics is microarray-based gene-expression profiling, a technology that provides comparative data on the transcription profiles of whole genomes.

An overview of the microarray technique

Expression microarrays are generally derived by printing or spotting cDNAs, or synthesizing oligonucleotides, onto glass or silicon slides or chips.[27] For cDNA arrays, cDNA clones amplified by polymerase chain reaction (PCR) are arrayed onto a solid support and a single array is cohybridized with fluorescently labeled cDNA probes derived from the experimental samples