

Mammalian Genetics and Genomics Program - July 2002

Li et al., Integrated platform for detection of DNA sequence variants using capillary array electrophoresis

(Li et al., *Electrophoresis*, 2002, 23, 1499-1511) Contact: C. T. Cuiat (865) 241-0672

We have developed a highly versatile platform that performs temperature gradient capillary electrophoresis (TGCE) for mutation/single-nucleotide polymorphism (SNP) detection, sequencing and mutation/SNP genotyping for identification of sequence variants on an automated 24-, 96- or 192-capillary array instrument. In the first mode, multiple DNA samples consisting of homoduplexes and heteroduplexes are separated by CE, during which a temperature gradient is applied that covers all possible temperatures of 50% melting equilibrium (T_m) for the samples. The differences in T_m results in separation of homoduplexes from heteroduplexes, thereby identifying the presence of DNA variants. The sequencing mode is then used to determine the exact location of the mutation/SNPs in the DNA variants. The first two modes allow the rapid identification of variants from the screening of a large number of samples. Only the variants need to be sequenced. The third mode utilizes multiplexed single-base extensions (SBEs) to survey mutations and SNPs at the known sites of DNA sequence. The TGCE approach combined with sequencing and SBE is fast and cost-effective for high-throughput mutation/SNP detection.

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Gene Rinchik, Dabney Johnson, Barry Berven, and Frank Harris of ORNL's Life Sciences Division traveled to Los Alamos National Laboratory for a July 10 and 11, 2002, meeting with Jill Trewell, Gary Resnick, Penny Hitchcock, and others participating in LANL's Biosciences Division investigations into host/pathogen interactions.

Drs. Rinchik and Johnson will make a return visit September 23 and 24, 2002, to attend a LANL-sponsored workshop addressing, among other topics, the role of genetic variation in susceptibility to infectious agents of potential use as bioweapons.