

identified about 15 million common DNA variants, mostly SNPs (199).

SNP is defined as a genomic locus where two or more alternative bases occur with appreciable frequency (>1%). SNPs are the most frequent type of variation in the human genome, occurring once every several hundred base pairs throughout the genome (200). For any given SNP, the SNP can occur in a coding region but not result in a change in amino acid, it can occur in a coding region with an amino acid change, it can occur in a regulatory region where the result is a change in gene expression, or it can occur in a region between genes.

### b. Examples of Lung Cancer, Colorectal Cancer, and Chronic Lymphocytic Leukemia

The practical utility of SNP analysis in the field of oncology is illustrated by the following. In brief, two SNPs within the *MMP-9* gene are associated with the risk of developing lung cancer with metastasis. To provide another example, SNPs within the *UGT1A7* have been shown to predict the response of colorectal cancer patients to capecitabine (201).

This concerns chronic lymphocytic leukemia (CLL). CLL has a heterogeneous clinical course. This variability in clinical course has stimulated interest in discovering prognostic biomarkers.

One such biomarker is mRNA encoding lipoprotein lipase. High levels of mRNA expression are associated with very poor prognosis for this type of cancer. However, detection of mRNA expression is not the same as detecting SNPs. In a study of SNPs in the gene encoding lipoprotein lipase, among 248 patients with CLL, Rombout et al. (202) focused on the SNP that is known as **rs13702**. CLL patients with the wild-type genotype (T/T) had very poor prognosis, while CLL patients with C/C genotype or T/C genotype had better prognosis.

The SNP **rs13702** is located at position 19868772 on human chromosome 8 (203). After transcription of the gene encoding for lipoprotein lipase, SNP **rs13702** resides in the 3'-untranslated region of the mRNA encoding lipoprotein lipase. The change in nucleotide in this SNP disrupts a regulatory element that functions with a species of miRNA, namely, miRNA-410. To provide a bit of scientific background, microRNAs (miR) are small 20–24-nucleotide noncoding RNAs that act as post-transcriptional inhibitors of gene expression by binding to miR recognition elements within the 3' UTR of their target mRNAs (204).

In their exploration of various SNPs and their possible association with survival time in CLL patients, Rombout et al. (205) concluded that, of the three SNPs in the lipoprotein lipase gene, rs301, rs328, and rs13702, it is the case

<sup>199</sup>Iacobucci I, et al. Use of single nucleotide polymorphism array technology to improve the identification of chromosomal lesions in leukemia. *Curr. Cancer Drug Targets* 2013;13:791–810.

<sup>200</sup>Engle LJ, et al. Using high-throughput SNP technologies to study cancer. *Oncogene* 2006;25:1594–601.

<sup>201</sup>Engle LJ, et al. Using high-throughput SNP technologies to study cancer. *Oncogene* 2006;25:1594–601.

<sup>202</sup>Rombout A, et al. Lipoprotein lipase SNPs rs13702 and rs301 correlated with clinical outcome in chronic lymphocytic leukemia patients. *PLoS One* 2015;0121526 (15 pp.).

<sup>203</sup>Deo RC, et al. Genetic differences between the determinants of lipid profile phenotypes in African and European Americans: The Jackson Heart Study. *PLoS Genetics* 2009;e1000342 (11 pp.).

<sup>204</sup>Richardson K, Nettleton JA, Rotllan N, et al. Gain-of-function lipoprotein lipase variant rs13702 modulates lipid traits through disruption of a microRNA-410 Seed Site. *Am. J. Hum. Genetics* 2013;92:5–14.

<sup>205</sup>Rombout A, et al. Lipoprotein lipase SNPs rs13702 and rs301 correlated with clinical outcome in chronic lymphocytic leukemia patients. *PLoS One* 2015; (15 pp.).