occurring in the gene coding regions (exons). Synonymous variations, which do not alter the amino acid sequence, were thought to be silent, but they can also influence mRNA splicing, mRNA stability, and protein conformation and function.

Changes in drug response often involve germline variations that affect the pharmacokinetics of an anticancer drug by reducing the expression or activity of coded enzymes. For instance, patients with acute lymphoblastic leukemia treated with 6-mercaptopurine and who have a homozygous deficiency in thiopurine *S*-methyltransferase enzyme activity have an extreme sensitivity to this drug as a result of the accumulation of higher cellular concentrations of thioguanine nucleotides. Consequently, they have an increased risk of myelosuppression and require a substantial dose reduction.[13] However, most drug response phenotypes respond to variations in multiple genes encoding proteins that are involved in drug absorption, transport, metabolism, elimination, and mechanism of action. The aggregate effect of multiple polymorphisms or alleles that are closely linked, known as a haplotype, is frequently inherited together and, fortunately, it can be considered as a functional unit that may be represented by a marker SNP. This property allows for large sections of the genome to be studied using relatively fewer marker SNPs. Unlike germline variations, somatic mutations are not present in normal cells and are not inheritable, and they can functionally be divided into driver and passenger. Most of them are temporary and do not contribute to cancer development, but driver mutations confer growth or survival advantages in cancer cells. When they are located in oncogenes, the cancer cells become "addicted" to their function, and the oncogenes may be the target of the therapy.[14]

The success of imatinib in the treatment of chronic myeloid leukemia paved the way for the development of treatments targeting genomic aberrations in solid tumors, an approach that has been especially effective in gastrointestinal stromal tumors, breast cancer, colorectal cancer, non-small cell lung cancer, and melanoma.[15] The International Cancer Genome Consortium, the Cancer Genome Atlas, and the Cancer Genome Project have afforded comprehensive genomic information on several cancer types and have identified genomic aberrations that are potentially targetable or associated with drug resistance, thus enabling a personalized approach to cancer therapy.[16]

3 EARLY DIAGNOSIS OF CANCER AND ITS THERAPEUTIC RELEVANCE

The high potential for mutation of tumor cells limits the usefulness of tissue biopsy as a standard prognostic procedure for cancer because, due to the genetic diversity within a single solid tumor, cells from one end may differ from those at the other and only some mutations are shared throughout the whole mass. Accordingly, a biopsy could miss mutations that might radically change the diagnosis and prognosis of a patient, and although it can provide data about specific mutations that might make a tumor vulnerable to targeted therapies, that information may become inaccurate as the cancer evolves.[17] For an early diagnosis, prognosis, and epidemiology of cancer, it is necessary to detect specific biomarkers that, ideally, should be collected from biofluids such as blood or serum. Several genetic, epigenetic, proteomic, glycomic, and imaging biomarkers are currently used for cancer diagnosis and therapeutic monitoring, including AFP (liver cancer), Bcr-Abl (chronic myeloid leukemia), BRCA1/BRCA2 (breast/ovarian cancer), BRAF V600E (melanoma/colorectal cancer), CA-125 (ovarian cancer), CA19-9 (pancreatic cancer), CEA (colorectal cancer), EGFR (non-small cell lung carcinoma), HER-2 (breast cancer), KIT (gastrointestinal stromal tumor), PSA (prostate cancer), and S100 (melanoma).[18] Although proteins are used in the clinic to diagnose illnesses and