(a) obtaining a third pair of CpG methylation datasets, with the first computing device, generated from the second cancerous biological sample and the third cancerous biological sample, wherein CpG methylation data generated from the second cancerous biological sample form a fifth dataset within the third pair of datasets, CpG methylation data generated from the third cancerous biological sample form a sixth dataset within the third pair of datasets, and the first, second, and third cancerous biological samples are different;

(b) generating a pair-wise methylation difference dataset, with a second processor, from the first, second, and third pair of datasets; and

(c) analyzing the pair-wise methylation difference dataset with a control dataset by a machine learning method to generate the cancer CpG methylation profile database, wherein

(1) the machine learning method comprises: identifying a plurality of makers and a plurality of weights based on a top score, and classifying the samples based on the plurality of markers and the plurality of weights; and

(2) the cancer CpG methylation profile database comprises a set of CpG methylation profiles and each CpG methylation profile represents a cancer type.

Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumors, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis, laryngeal cancer, lip cancer, liver cancer, Lymphoid Neoplasm Diffuse Large B-cell Lymphoma [DLBCL), malignant fibrous histiocytoma bone cancer, medulloblastoma, medullo epithelioma, melanoma, Merkel cell carcinoma, Merkel cell skin carcinoma, mesothelioma (MESO), metastatic squamous neck cancer with occult primary, mouth cancer, multiple endocrine neoplasia syndromes, multiple myeloma, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic syndromes, myeloproliferative neoplasms, nasal cavity cancer, nasopharyngeal cancer, neuroblastoma, Non-Hodgkin lymphoma, nonmelanoma skin cancer, non-small cell lung cancer, oral cancer, oral cavity cancer, oropharyngeal cancer, osteosarcoma, other brain and spinal cord tumors, ovarian cancer, ovarian epithelial cancer, ovarian germ cell tumor, ovarian low malignant potential tumor, pancreatic cancer, papillomatosis, paranasal sinus cancer, parathyroid cancer, pelvic cancer, penile cancer, pharyngeal cancer, pheochromocytoma and paraganglioma (PCPG), pineal parenchymal tumors of intermediate differentiation, pineoblastoma, pituitary tumor, plasma cell neoplasm/multiple myeloma, pleuropulmonary blastoma, primary central nervous system (CNS) lymphoma, primary hepatocellular liver cancer, prostate cancer such as prostate adenocarcinoma (PRAD), rectal cancer, renal cancer, renal cell (kidney) cancer, renal cell cancer, respiratory tract cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, sarcoma (SARC), Sezary syndrome, skin cutaneous melanoma (SKCM), small cell lung cancer, small intestine cancer, soft tissue sarcoma, squamous cell carcinoma, squamous neck cancer, stomach (gastric) cancer, supratentorial primitive neuroectodermal tumors, T-cell lymphoma, testicular cancer testicular germ cell tumors (TGCT), throat cancer, thymic carcinoma, thymoma (THYM), thyroid cancer (THCA), transitional cell cancer, transitional cell cancer of the renal pelvis and ureter, trophoblastic tumor, ureter cancer, urethral cancer, uterine cancer, uterine cancer, uveal melanoma (UVM), vaginal cancer, vulvar cancer, Waldenstrom macroglobulinemia, or Wilm's tumor.

23. The computer-implemented method of claim 14, wherein the biological samples comprise a circulating tumor DNA sample or a tissue sample.