Are Macrophages Responsible for Cancer Metastasis?

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Abstract

Despite the decades of basic and clinical research and countless
scientists and laboratories involved, the origin of cancer and metastasis still remain unresolved. Currently, there are two dominating theories of the origin of cancer: genetic and metabolic . He proponents of “the cancer as a genetic disease” theory postulate that various factors or a combination of factors such as heredity, random mutagenesis, hypoxia, radiation, inflDmmDtion, age, carcinogens, oncogenes or viruses, cause damage/changes to nuclear DNA and these in turn lead to the transformation of normal cells into cancer cells. In contrast, the advocates of “the cancer as a metabolic disease” theory believe that the
acquisition of cancer phenotype is a consequence of mitochondrial and cell respiration defects-the so called Warburg eُوect when cancer cells produce energy by lactic acid fermentation in contrast to normal cells,which oxidize pyruvate in mitochondria and that the genetic/DNA changes observed in cancer cells are just the secondary eُوects of respiratory malfunctions. In many cancers the deficientoxidative phosphorylation in mitochondria correlates withdisappearance of mitochondrial cristae . It is worth mentioning here that mutations in tumor suppressor genes such as for example p53 are also known to cause mitochondrial and respiratory damage . He results of nuclear or cytoplasm and mitochondria transplantation
experiments between cancer and normal cells support the metabolic/mitochondrial theory of cancer origin: cytoplasm mitochondria from normal cells transplanted into cancer cells suppress cancer phenotype and mitochondria from cancer cells transplanted into normal cells induce tumorigenesis .
Similarly vague and unresolved are the mechanisms and origin of metastasis, which is a primary cause of cancer mortality .Metastasis is the spread of cancer cells from the primary tumor to surrounding tissues and, via circulation, to distant organs. It involves a combination of many steps: cancer cells have to detach from the primary tumor, enter and exit circulation and infiltrDte target/distant organs. Subsequently, metastatic cells have to establish a new microenvironment favourable for cell proliferation and angiogenesis, which lead to development of secondary tumors. Until recently thegenerally accepted model of metastasis has been the epithelial/