Nitric oxide (NO) is a signaling free radical that is produced by NO synthases. Two constitutive isoforms (endothelial and neuronal) and one inducible (iNOS) isoform of the NO synthases produce NO upon physiological and pathophysiological stimuli. iNOS expression is commonly associated with malignant disease. However, the role of iNOS during tumor development is highly complex, and not completely understood. iNOS expression levels and associated NO production in the tumor microenvironment may result in pro-tumor or anti-tumor activities. High levels of NO produced by iNOS stimulated by inflammatory cytokines in macrophages often result in cytostatic and/or cytotoxic effects on tumor cells. On the other hand, low concentrations of NO produced by constitutively expressed iNOS in tumor cells may be associated with their progression.

To determine the importance of iNOS in colon cancer progression we used human colon carcinoma cell lines derived from the same patient: SW480 obtained from the primary tumor, and SW620 derived from the lymph node metastatic site.

Regarding the expression levels of iNOS, SW620 cells displayed higher iNOS expression levels as compared to the levels determined for SW480 cells. To assess the importance of NO in tumor progression, expression of iNOS was knocked down in SW620 cells using permanent transfection with shRNA.

Silenced iNOS SW620 cells feature diminished expression of genes associated with angiogenesis, proliferation, hypoxia and multidrug resistance. These cells over-express p21Waf, a tumor suppressor gene, and are positive for e-cadherin expression. Lower expression levels of β-catenin and vimentin were detected in silenced iNOS SW620 cells.

They resemble the primary tumor cells SW480 in many ways and corroborates with the importance of iNOS and NO generation for the development of colon carcinoma.