ENDOGENOUS ANGIOGENESIS INHIBITORS: DO THESE MOLECULES SUPPRESS ANGIOGENESIS-DEPENDENT DISEASE?

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Since 1980, more than 20 endogenous angiogenesis inhibitors have been discovered in the circulation or in extracellular matrix (1) (2). A novel organizing principle for understanding a basic mechanism of diseases which themselves appear to be unrelated, is to analyze deficiencies of endogenous angiogenesis inhibitors. For example, for many cancers, the switch to the angiogenic phenotype is preceded by downregulated expression of thrombospondin-1 in the tumor bed (3); in rheumatoid arthritis there is a deficiency of endostatin in the joint fluid; the persistent hyaloid blood vessels which result in blindness at birth in Knobloch’s syndrome are caused by a mutation in endostatin (4); and infantile hemangiomas have a deficiency of interferon alpha which normally suppresses bFGF (5). For other diseases, upregulation of an endogenous angiogenesis inhibitor protects against certain diseases. Endostatin is elevated in individuals with Down syndrome, who are the most protected against cancer of all humans (6).

We are currently investigating the possibility that other diseases such as cerebral hemorrhage and retinal neovascularization in premature babies may be due to a deficiency of 2-methoxyestradiol. Conclusion: Certain angiogenesis-dependent diseases have been identified in almost every speciality of medicine (7). From a therapeutic standpoint it may be prudent to think about these pathologies, not only in terms of overexpression of positive angiogenesis regulators, but also as local or systemic deficiencies of negative angiogenesis regulators.