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Osteopontin splice variants are cancer progression markers

The early detection of tumor dissemination is a challenge in cancer diagnosis because biomarkers for invasiveness are largely lacking in clinical medicine. Osteopontin is frequently secreted by cancer cells and plays important roles in their ability to metastasize. Despite a sizeable and continuously growing literature on osteopontin and cancer the molecule has not yet found entry into diagnostics. Osteopontin is subject to alternative splicing, which yields three messages, Osteopontin-a, -b, and -c. The shortest form, Osteopontin-c is selectively expressed in invasive, but not in non-invasive, breast tumor cell lines, and it effectively supports anchorage independence. Osteopontin-c is present in 75-80% of breast cancers and 0% of normal breast tissues. Our identification of Osteopontin variants that are more specific for cancer than the full-length transcript has opened new possibilities for measuring them in the blood as a means of early detection. We have developed a real-time RT-PCR blood test and evaluated it in a pilot study of breast, lung, pancreatic, gynecologic, and other cancers, compared to non-cancer controls. Osteopontin-b was increased in lung cancers and pancreatic cancers. When applying a cutoff of 2 standard deviations above normal, elevation in osteopontin-b transcripts detected over 40% of lung cancers. Osteopontin-c was increased in gynecologic and pancreatic cancers. Elevation in osteopontin-c also detected a fraction of breast cancers and lung cancers, suggesting heterogeneity within those types of tumors. Specifically, breast carcinomas were associated with significantly higher levels of osteopontin-c mRNA in the blood than carcinomas in situ. Osteopontin-b and -c in the blood are biomarkers for distinct cancers.

Biography
Georg F. Weber attended medical school in Wuerzburg, Germany. He worked at the Dana-Farber Cancer Institute, Harvard Medical School from 1990 through 1999 and is currently on the faculty at the University of Cincinnati. He has published over 70 scientific reports, including many in the most respected professional journals, and various monographs, most recently a textbook on molecular oncology. He holds several patents. As a component of his mission to research cancer dissemination, he is the Founder and Chief Executive Officer of MetaMol Theranostics, a company specialized in diagnosis and treatment of cancer metastasis.

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