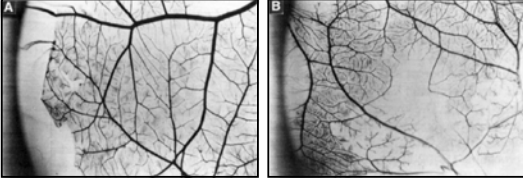


Inhibitor Discovery

- **Cartilage-derived Inhibitor (CDI)**
(Moses MA, Sudhalter J, Langer R. *Identification of an inhibitor of neovascularization from cartilage.* Science 1990)
- **Chondrocyte-derived Inhibitor(ChDI)**
(Moses MA, Sudhalter J, Langer R. *Isolation and characterization of an inhibitor of neovascularization from scapular chondrocytes.* J. Cell. Biol. 1992)
- **Troponin I (TnI)**
(Moses MA, Wiederschain D, Wu I, Fernandez CA, Ghazizadeh V, Lane WS, Flynn E, Sytkowski A, Tao T, Langer R. *Troponin I is present in human cartilage and inhibits angiogenesis.* Proc. Natl. Acad. Sci. 1999)
- **Angiostatin**
(O'Reilly MS, Holmgren L, Shing Y, Chen C, Rosenthal RA, Moses MA, Lane WS, Cao Y, Sage EH, Folkman J. *Angiostatin: A novel angiogenesis inhibitor that mediates the suppression of metastases by a Lewis lung carcinoma.* Cell 1994)
- **Heparinase**
(Sasisekhara R, Moses MA, Nugent MA, Cooney C, Langer R. *Heparinase is an inhibitor of neovascularization.* Proc. Natl. Acad. Sci. 1994)
- **Loop 6 / TIMP-2**
(Fernandez CA, Butterfield C, Jackson G, Moses MA. *Structural and functional uncoupling of the enzymatic and angiogenic inhibitory activities of TIMP-2: Loop 6 is a novel angiogenesis inhibitor.* J. Biol. Chem. 2003)
- **Matrilin 1**
(Foradori MJ, Chen Q, Tsang PCW, Langer R, Moses MA. *Matrilin-1: A potential regulator of angiogenesis.* AACR Annual Meeting, Washington, DC, April 2006)

**A Cartilage-Derived TIMP Inhibits
Angiogenesis *in vivo***



Moses, M.A., Sudhalter, J. and Langer, R., *Science*, 246: 1408-1410, 1990

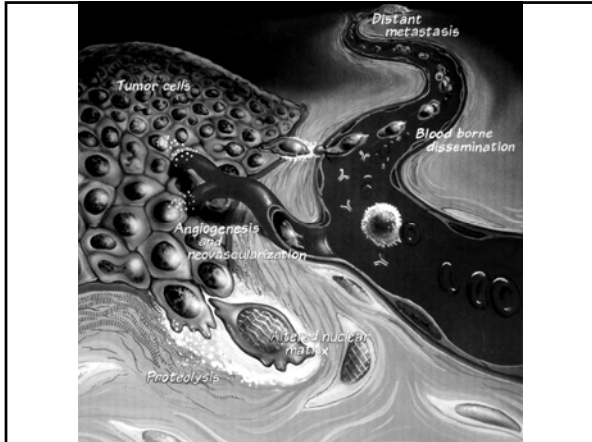
February 28, 2004

“Anti-angiogenic therapy can now be considered the **4th modality** for cancer treatment” (in addition to surgery, radiation and chemotherapy).

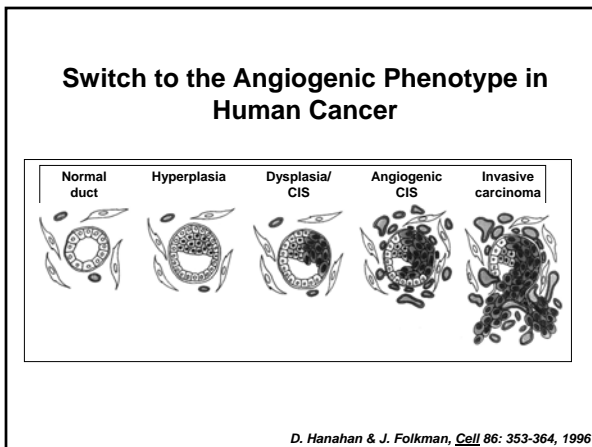
*Mark McClellan
FDA Commissioner*

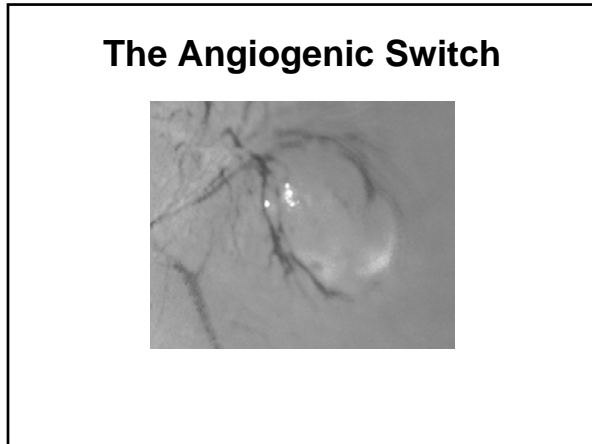
“Treatments to stimulate or repress angiogenesis will eventually benefit half a billion people worldwide.”

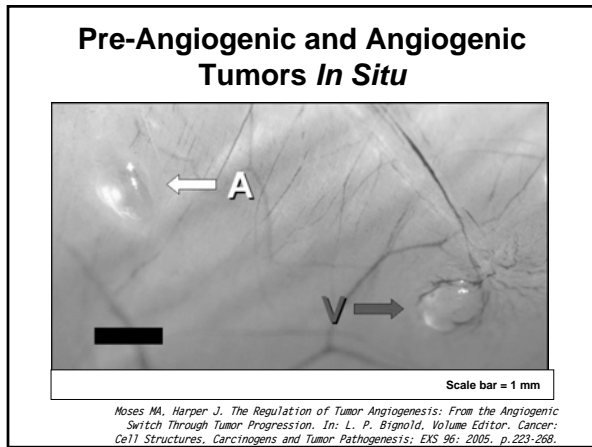
P. Carmeliet, Nature 438:932-936, 2005

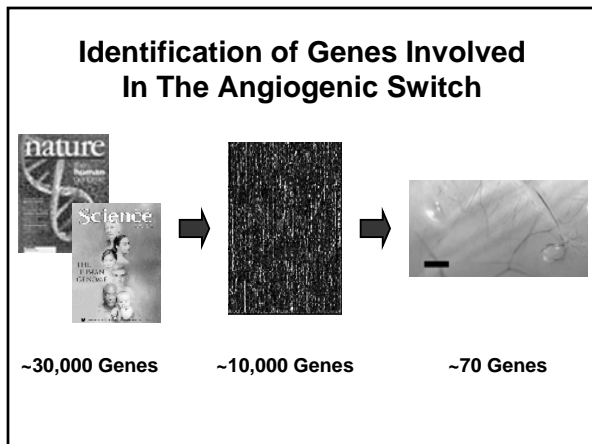


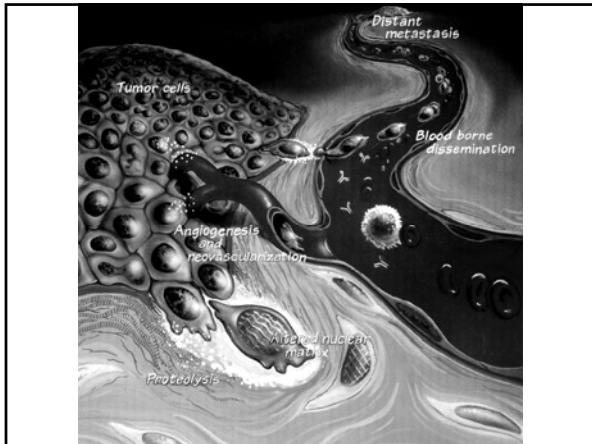
The Angiogenic Switch









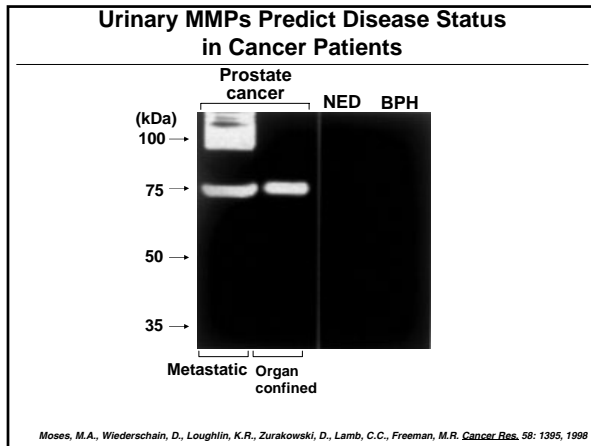


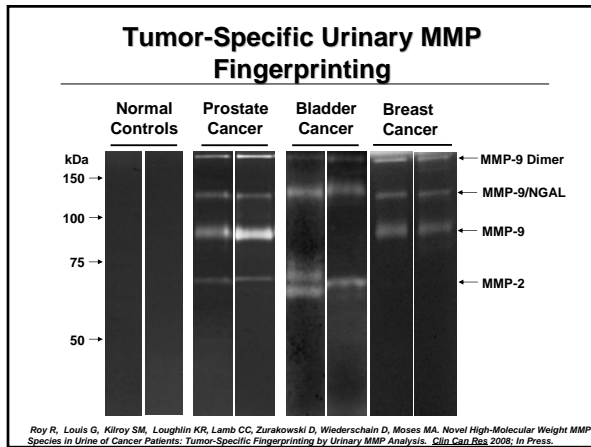
Discovering Cancer Biomarkers: Urinary Proteomics

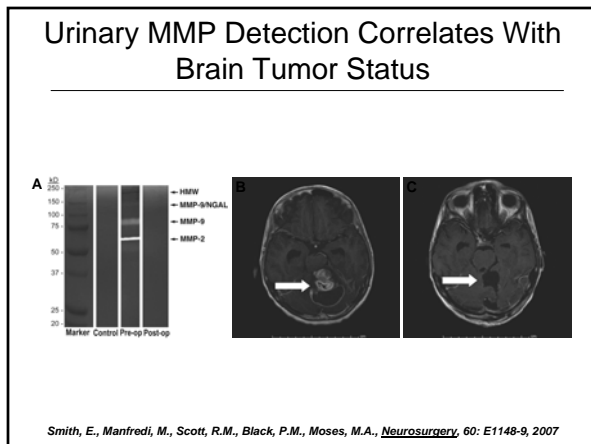
*From Cancer Diagnosis and
Prognosis Through Therapy*

Why Urine?

- Non-invasive
- Far fewer proteins relative to other body fluids such as serum or plasma, therefore a much lower background of “contaminating proteins”
- Profile of the human urinary proteome is known to change as a result of disease
- Urine can be easily adapted to high throughput diagnostic and prognostic techniques







Journal of Clinical Oncology, 22: 499, February 2004

Urinary VEGF and MMP Levels As Predictive Markers of 1-Year Progression-Free Survival in Cancer Patients Treated With Radiation Therapy: A Longitudinal Study of Protein Kinetics Throughout Tumor Progression and Therapy

Linda W. Chan, Marsha A. Moses, Elizabeth Goley, Mary Sproull, Thierry Muanza, C. Norman Coleman, William D. Figg, Paul S. Albert, Cynthia Ménard, and Kevin Camphausen

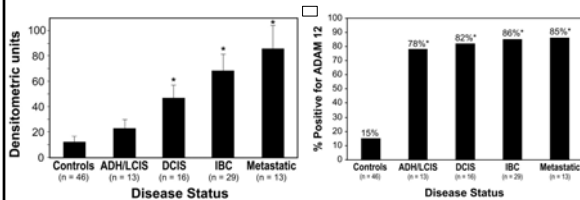
In 242 patients with prostate cancer, compared to healthy controls (age and sex-matched), urinary MMPs predicted **1-year progression-free survival**.

JBC Papers in Press, published on September 20, 2004 as Manuscript M409565200

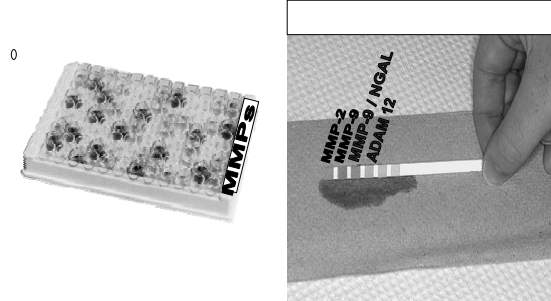
ADAM 12 Cleaves ECM Proteins: Correlation with Cancer Status and Stage

Roopali Roy^{1,4}, Ulla M. Wewer⁵, David Zurakowski^{2,4}, Susan E. Pories^{3,4} and Marsha A. Moses^{1,4,*}

- ADAM 12 is a **metalloproteinase** which can be detected in the **urine** of women with early breast cancer (intraductal **carcinoma in situ**) and correlates with breast cancer progression.



Urinary Biomarkers
Novel Cancer Prognostics/Diagnostics





“Judah Folkman’s fiercely original and courageous intelligence, his gift for focusing on big, important questions that could make a difference in people’s lives, and his delight in discovery, inspired hundreds of scientists, clinicians, and patients all over the world. We are honored and grateful to have been witness to his genius and his selflessness.”

***Cancer Cell*, February 13, 2008
M. Klagsbrun and M. A. Moses**

