

Obituary

Judah Folkman

(1933–2008)



The founder of the field of angiogenesis research, Professor Judah Folkman, passed away unexpectedly on January 14, 2008, a few weeks before his 75th birthday. The scientific community has lost a great scientist and a truly inspiring and visionary mind. His famous article from 1971 published in the *New England Journal of Medicine* did not just hypothesize the angiogenesis-dependency of malignant tumor growth, rather, Folkman (i) predicted that tumors

would be restricted to microscopic size in the absence of angiogenesis, (ii) suggested that tumors secrete diffusible angiogenic molecules, (iii) described a model of tumor dormancy due to blocked angiogenesis, (iv) proposed the term anti-angiogenesis for the prevention of new capillary sprouts from being recruited into a growing tumor, (v) envisaged the future discovery of angiogenesis inhibitors, and (vi) proposed the idea that an antibody to a tumor angiogenic factor could be an anti-cancer drug. In the 37 years since then, all of these proposals have become reality.

Yet, it was a bumpy road. What appears so self-evident today was met with scepticism, criticism, and open rejection. Being the positive thinker that he was, Folkman laughingly referred later to these bittersweet early days of angiogenesis research as a great opportunity, because “it has given us a 15 year competitive advantage“. He also has publicly contemplated about “the fine line between perseverance and obstinacy“. Everybody in the angiogenesis community knows that neither this scientific field nor the clinical translation of angiogenesis research would be anywhere close to where they are today if it hadn't been for this one outstanding scientist.

The scientific contributions of Professor Folkman's laboratory are too numerous to be listed here. His laboratory has developed relevant animal models of angiogenesis, pioneered the culture of endothelial cells, identified bFGF as the first angiogenic factor, purified VEGF independently at the same time as Napoleone Ferrara from Genentech (published 1990 in *Growth Factors*), pursued the first preclinical anti-angiogenesis experiments to treat cancer, and identified the first endogenous inhibitors of

angiogenesis. Equally important as his scientific contributions was the impact of his charismatic personality in shaping the field. His lab has trained numerous scientists that have become leaders in the field. Yet, he has also had great impact on people who have never worked directly with him. Quite a few senior scientists have anecdotes to tell how a single public lecture or a private conversation changed their future scientific career and the direction of their work.

The FDA approval of the VEGF neutralizing antibody Bevacizumab (Avastin) in 2004 was the critical litmus test for the field. It provided the ultimate proof that angiogenesis research is not just a fascinating scientific discipline whose knowledge can be used to cure cancer-bearing mice. Instead, the predictions of the 1971 *New England Journal of Medicine* article have become reality, and anti-angiogenesis therapy has changed the way tumors are treated. Moreover, anti-angiogenesis as predicted by Folkman is not just a novel anti-tumor therapy, but also holds great prospect for non-neoplastic diseases. The clinical approval of anti-VEGF therapies to treat age-related macular degeneration is considered the most important advance in the field of ophthalmology in the last 30 years. As such, Folkman's concepts and experiments have paved the way for a paradigm shift in biomedicine. The long-term impact of this shift can presently only vaguely be anticipated. A review by Peter Carmeliet in *Nature* (Dec. 2005) concluded that “angiogenesis research will probably change the face of medicine over the next decades with more than 500 million people worldwide predicted to benefit from pro- or anti-angiogenesis treatment“.

The complexity of modern biomedical research makes it increasingly difficult to attribute important discoveries to individual scientists. However, it is still individual scientists who make the difference. Judah Folkman is truly a shining example of a scientist and clinician who has made a difference. His accomplishments have been recognized by 147 awards and prizes including 19 honorary degrees. Yet, it will surely be asked if during his lifetime he received the recognition that he deserved.

The field of angiogenesis research has lost its founding father. This is a moment of deep sadness. Professor Folkman's legacy will be alive for generations of vascular biologists to come.

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