Jorgen Fogh – 1923-1984 – A Tribute

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I read a lot of cell culture papers. The earliest journal article in my files dates back to 1911 ("Cultivation In Vitro of Malignant Tumors", by Alexis Carrel and Montrose Burrows). The old papers are well worth reading as the foundation of today's cell culture – why we do things in a certain way, why cell lines behave the way they do. In my reading, I began to notice one person's name appearing over and over again. "Jørgen Fogh" appears in bibliographies and cell line catalogues alongside many of the cell lines that laboratories use today – HT-29 from colorectal cancer, Caki-1 from renal cancer, Calu-1 from lung cancer.

Who was Jørgen Fogh? How did his name come to be associated with so many cell lines?

SEARCHING FOR JØRGEN FOGH

In 1986, an invited review by Jørgen Fogh appeared in the journal Cancer Investigation [1]. The review was published posthumously and was accompanied by an *In Memoriam* tribute, written by Yashar Hirshaut [2]. Looking at Hirshaut's tribute, we learn that Fogh was born in Copenhagen, Denmark in 1923 and attended the University of Copenhagen where he received an MD summa cum laude. Fogh trained in obstetrics and gynecology before moving to the United States in 1953. After time spent at the University of California, Berkeley, New York State Department of Health, and Roswell Park Memorial Institute, Fogh started work at the Sloan-Kettering Institute in 1960. He was to work at Sloan-Kettering for more than 20 years, until his death on 27 December 1984.

Fogh was recognized for many achievements over his career. He became a professor of cell biology at the Cornell University Graduate School of Medical Sciences in 1984, and received the William Nielsens Fond Award for his "most significant accomplishments in cancer research" in 1983. Fogh wrote numerous publications and edited four books: *Contamination in Tissue Culture*, Academic Press 1973; *Human Tumor Cells in Vitro*, Plenum Press 1975; and with Beppino Giovanella, *The Nude Mouse in Experimental and Clinical Research*, Academic Press, Vol. 1 in 1978 and Vol. 2 in 1982.

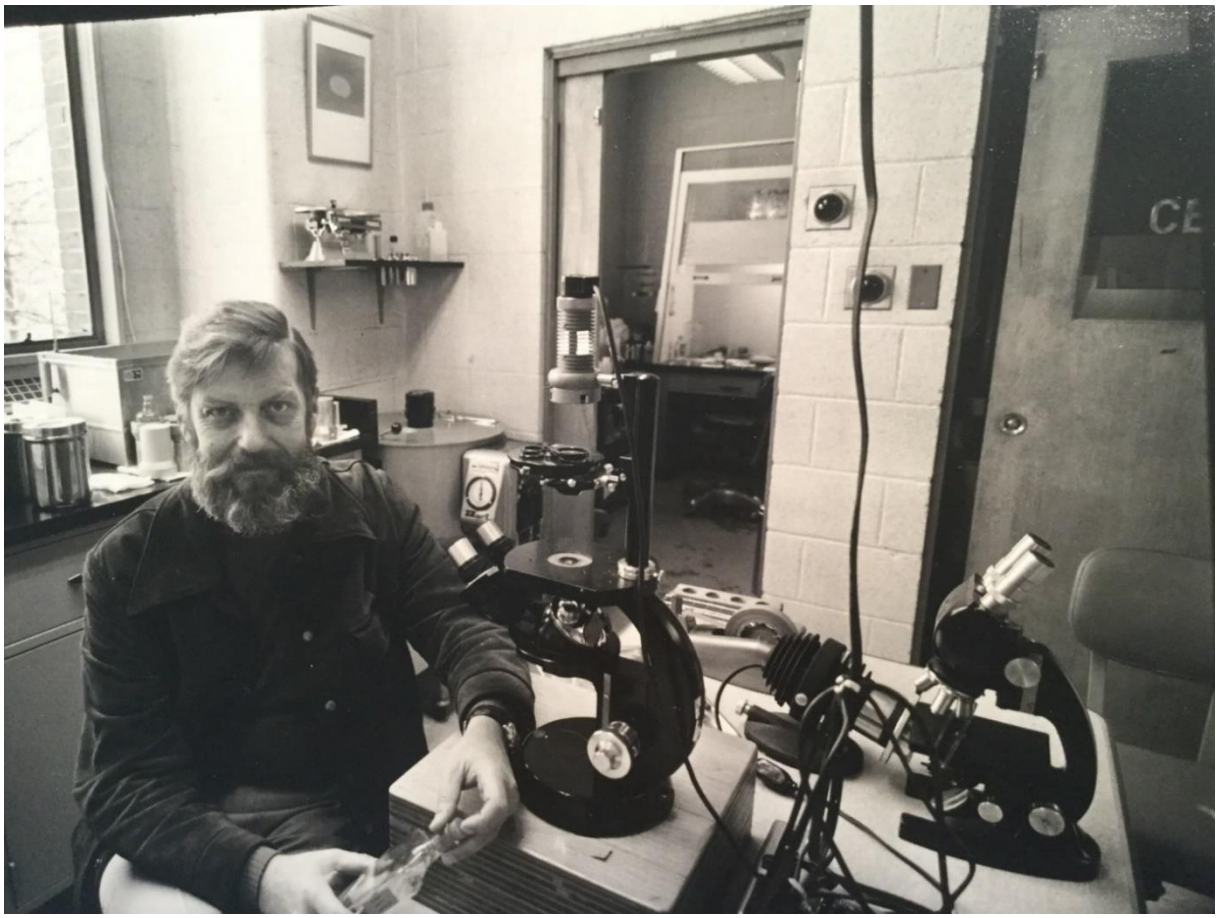
Jørgen Fogh was remembered as a "warm, kind and reliable friend and a person who cared for others" [2]. He worked closely with his wife, Helle Fogh, who was an accomplished cytogeneticist. Hirshaut finished his tribute very simply, saying "We will all miss him"

SEARCHING FOR CELL LINES

Fogh was clearly fascinated by human tumor cell lines and their importance for cancer research. His laboratory spent more than 20 years working to establish cell lines from many different cancer types, and operated a cell bank where their cultures were stored and characterized. In 1986, Fogh published a list of 329 human cell lines that were available at the Human Tumor Cell Line Bank, either established in their laboratory or shared by colleagues who sent their cell lines for storage and characterization [1]. These 329 cell lines were selected from an even larger collection, based on the absence of detectable contamination and ready growth in culture.

How many cell lines did Jørgen Fogh establish? It is difficult to know for sure. A number of colleagues at Sloan-Kettering Institute collaborated together to establish and study tumor cell lines. Looking at the "Tangible Materials available for Licensing" on the Memorial Sloan-Kettering website [3], Fogh's name is listed as the originator or inventor of 16 cell lines that remain available at his institute. Analysis of some of Fogh's papers [4, 5, 6, 7, 8] brings this total to 34 cell lines where "J. Fogh" is listed as their originator.

There are pitfalls when trying to establish cell lines in culture. In the 1960s, Fogh recognized the importance of mycoplasma contamination and production of SV40 virus in cell lines in vitro [9, 10]. Then Stanley Gartler discovered that many of the cell lines in use at that time were misidentified and were actually HeLa [11]. Fogh was to spend the next decade exploring this finding in his own collection.



Gartler discovered that HeLa could be detected using a small number of isoenzyme markers; HeLa cells carry G6PD A, an isoenzyme variant that is common in individuals of African descent but is unusual in other populations [11]. HeLa could also be detected using cytogenetic analysis due to the presence of unique "HeLa marker" chromosomes [12]. However, these techniques did not always work when applied to other cell lines. For example, Fogh investigated a set of six cell lines that all shared the same donor origin [13]. Four of the six cell lines were misidentified, but this was not picked up using "HeLa markers" because all six cell lines carried G6PD B (i.e., they were not HeLa).

Fogh worked with colleagues including William Wright, Nicholas Dracopoli, and Marilyn Pollack to improve authentication testing methods. They expanded the number of markers that were used for isoenzyme analysis to improve discrimination between cell lines [7, 8] and explored new methods such as HLA analysis [14]. Fogh and Dracopoli examined cell lines over time and found that loss of heterozygosity occurred in many cultures as they were passaged [15]. Modern authentication testing (e.g., STR and SNP genotyping) continues to benefit from these discoveries. For a test method to be successful, scientists must determine how many loci will give good discrimination between cell lines and how to interpret results when genetic drift occurs with passaging.

Scientists in this field tend to be remembered for discovering misidentified cell lines – the "imposters" of the cell culture world. But Fogh knew that it is equally important to demonstrate that cell lines are good models so that the research community can continue to use them. For example, scientists in the 1980s were studying stem cell behavior in the TERA2 cell line and were concerned about one of its derivatives, NTERA2, which was displaying unexpected behavior. Fogh was able to use his improved testing methods to prove that NTERA2 was authentic [16]. NTERA2 went on to become an important model for stem cell pluripotency and neuronal differentiation [17].

We might think about stem cell culture as a "new" technique, but in reality, everything in cell culture rests on the work of the colleagues who have gone before us. Work performed by Jørgen Fogh in the 1970s and 1980s continues to underpin our research today, which is part of his legacy.

ACKNOWLEDGEMENTS

I would like to thank Jens and Peter Fogh for providing the photographs of Jørgen Fogh that appear in this article.

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Cell lines established by Jørgen Fogh

Ast-1 (CVCL_LK72)	Caco-2 (CVCL_0025)	Caco-3 (CVCL_QW78)
Caki-1 (CVCL_0234)	Caki-2 (CVCL_0235)	Cali-1 (CVCL_RP61)
Calu-1 (CVCL_0608)	Calu-2 (CVCL_1E46)	Calu-3 (CVCL_0609)
Calu-6 (CVCL_0236)	Cama-1 (CVCL_1115)	Caov-1 (CVCL_0200)
Caov-3 (CVCL_0231)	Caov-4 (CVCL_0202)	Capan-1 (CVCL_0237)
Capan-2 (CVCL_0026)	Casa-1 (CVCL_1E91)	Cates-1B (CVCL_3296)
Esa-1 (CVCL_J512)	HT-3 (CVCL_1293)	HT-29 (CVCL_0320)
HT-144 (CVCL_0318)	Ins-1 (CVCL_VK12)	Malme-3M (CVCL_1438)
Malme-3S (CVCL_1E90)	Nemo-1 (CVCL_1E49)	Safi-1 (CVCL_1E92)
SaOS-1 (CVCL_1E51)	SaOS-2 (CVCL_0548)	SK-HEP-1 (CVCL_0525)
SK-NEP-1 (CVCL_0631)	Tera-1 (CVCL_2776)	Tera-2 (CVCL_2777)
Wiltu-1 (CVCL_B481)		