

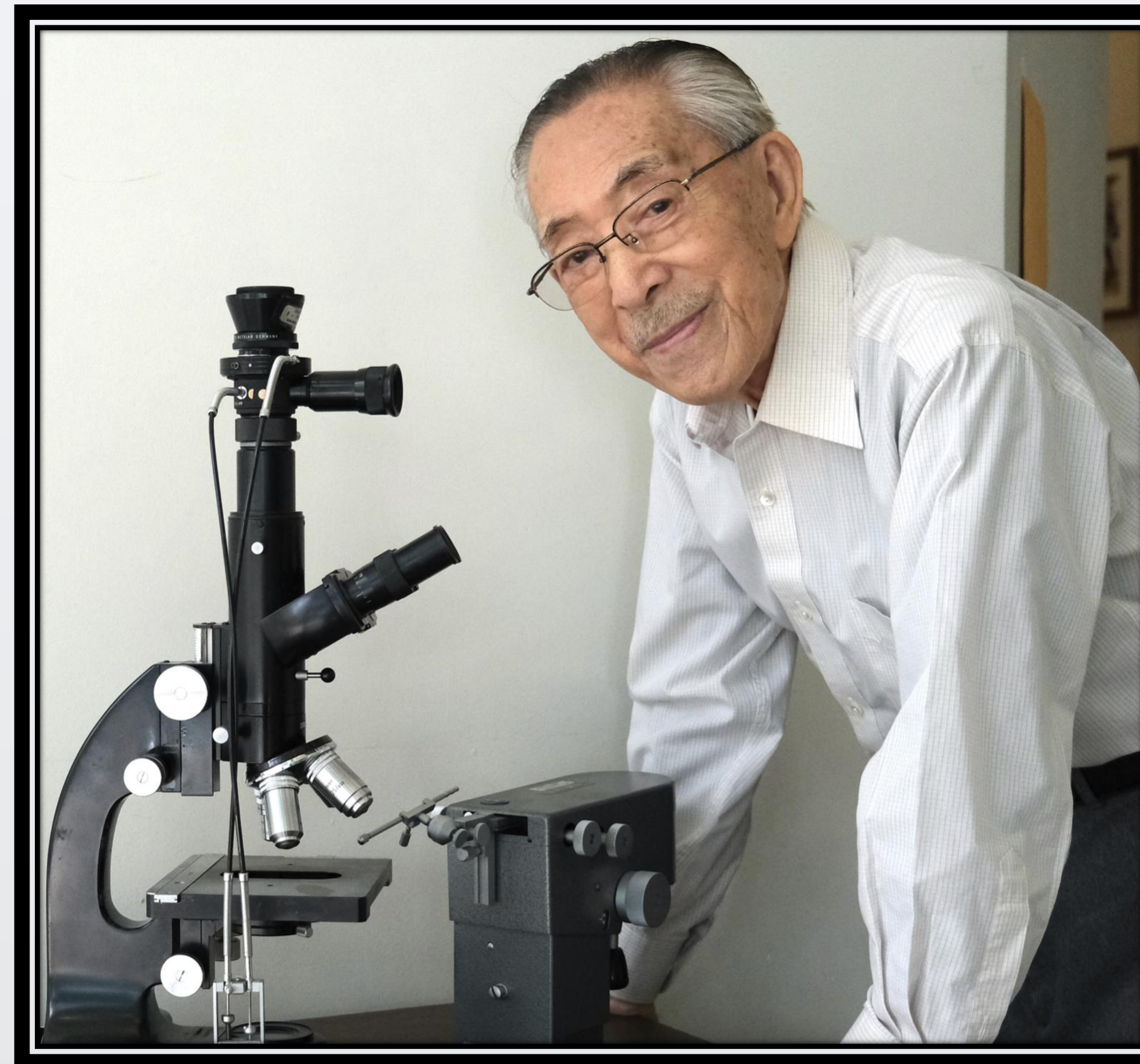
## Ryuzo 'Yana' Yanagimachi Ph.D. 1928 - 2023

### Career

- 1953 BS Biology, Hokkaido University, Japan
- 1960 PhD, Embryology, Hokkaido University
- 1960 – 1964 Postdoctoral Position with M.C. Chang at Worcester Foundation for Experimental Biology, Shrewsbury, MA
- 1964 – 1966 Research Associate, Faculty of Science, Hokkaido University
- 1966 – 2023 Professor, John A. Burns School of Medicine, University of Hawai'i at Manoa (59 years!)
- Greater than 400 publications
- Sixty-two publications in Nature, Science, and PNAS
- 72 publications in BOR
- Manuscripts have been cited over 47,000 times

### Awards and Recognitions

- Awarded the International Prize for Biology (Japan), "The Emperor's Award" in 1996
- Carl G. Hartman Award, SSR, 1999
- Pioneer Award, IETS, 2000
- Elected to the National Academy of Sciences in 2001
- Elected to the Hall of Honor of the NICHD in 2003
- Awarded the Kyoto Prize in 2023
- H-index is 108 with 47,563 citations



**The Father of *In Vitro* Fertilization**

### Yana in his own words

- During a laboratory session in an animal embryology course at the university's marine laboratory, I witnessed the moment of sea urchin fertilization and egg activation, followed by rapid embryo development. It was then that I chose fertilization and development as the subject of my bachelor of science thesis research.
- Research never ends. The more we study, the more we find problems to be solved.
- Undoubtedly, reproductive biologists will make many exciting discoveries during the 21st century. Entirely new technologies that cannot be foreseen today will be developed. Whenever new discoveries and novel inventions are made, it is important to fully inform the general public what their implications are and how they will affect and contribute to the advancement of human knowledge and welfare.
- Yanagimachi, R. (2009). Germ cell research: a personal perspective. *Biol Reprod*, 80(2), 204-218.
- "Be OUTSTANDING, Excellent is not enough"

### Highlights of Yana's Distinguished Research Career

#### In Vitro Sperm Capacitation

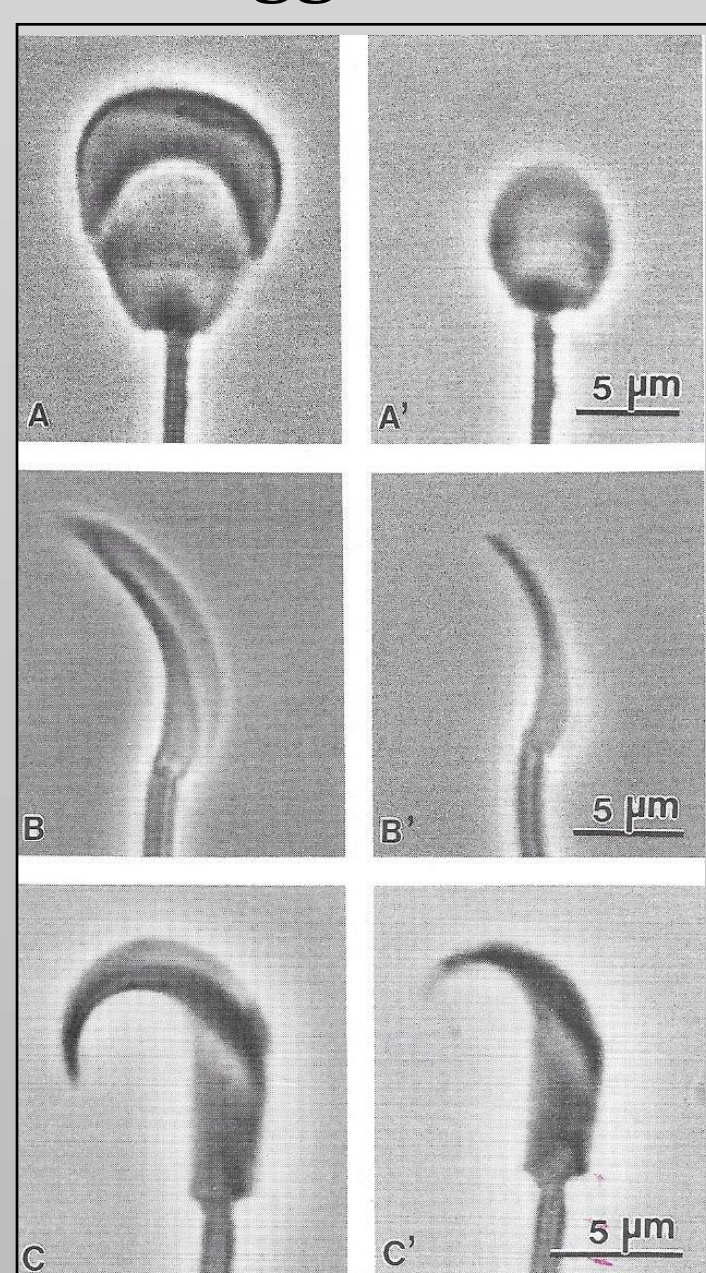
- Yana's first major contribution to the field of reproduction was in 1963 and 1964.
- Yana and Dr. Chang achieved the first in vitro fertilization of a rodent (hamster).
- This was also the first report of capacitation in vitro.

#### Hyperactivation of Spermatozoa

- Yana made an observation while studying capacitation that spermatozoa became extremely motile before the acrosome reaction.
- He coined the observation "hyperactivation".
- This hyperactivation is speculated to aid the sperm to move up the oviduct in a chemoattractant manner and in penetrating the zona pellucida of the egg.

#### Sperm Acrosome Reaction

- Yana discovered that the plasma membrane over the equatorial segment of the acrosome was the region that fused with zona pellucida of the egg.

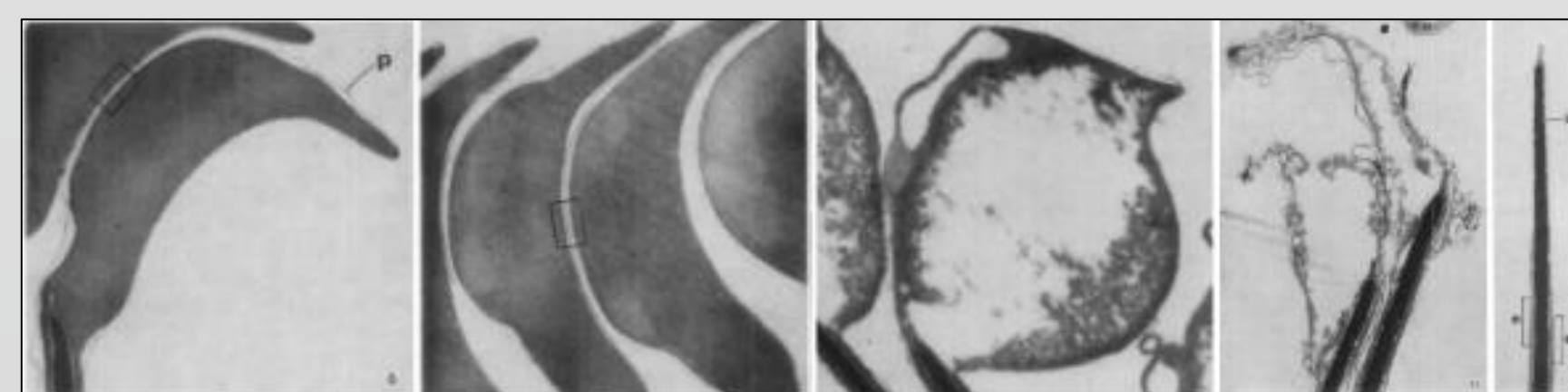


Phase-contrast micrographs of guinea pig (A), Chinese hamster (B), and golden hamster (C) spermatozoa before and after the acrosome reaction.

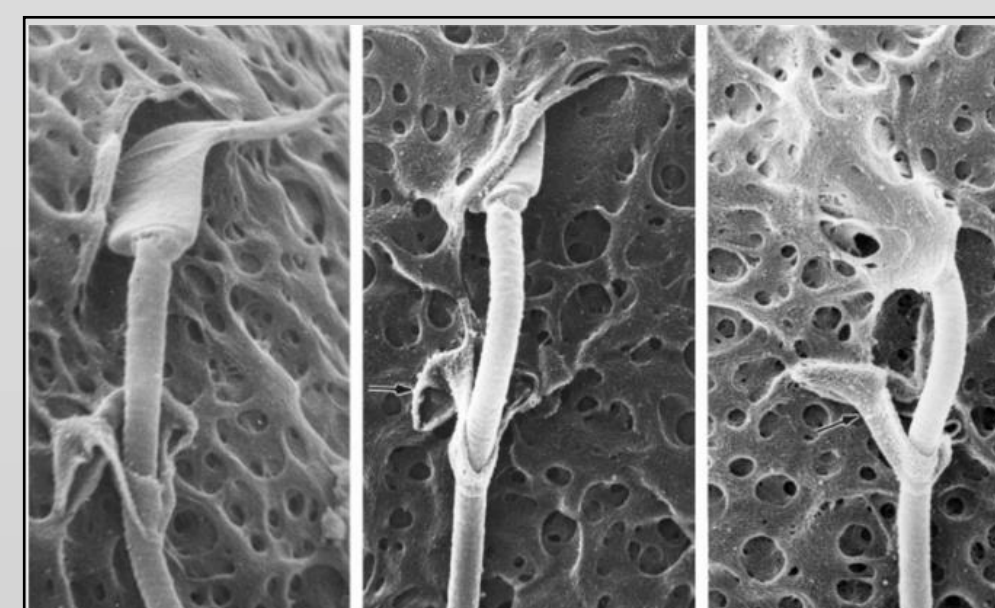
Yanagimachi R. Mammalian fertilization. In: Knobil E, Neill JD (eds.), *The Physiology of Reproduction*, vol. 1. New York: Raven Press; 1994: 189–317.

#### Calcium Ions are Essential for Fertilization

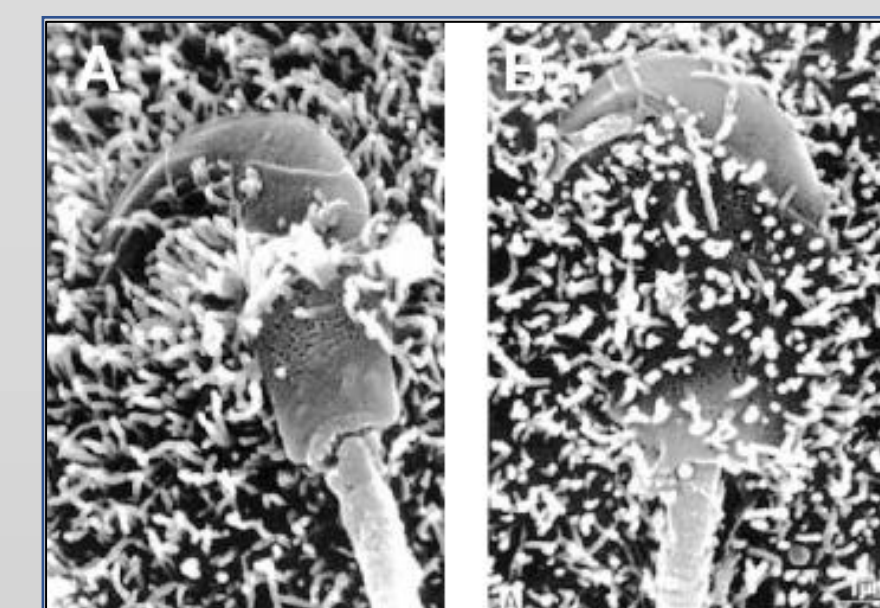
- Yana learned as an undergraduate student that sea urchin fertilization required seawater with  $Ca^{2+}$  ions.
- Yana reported that  $Ca^{2+}$  had an important role in many steps of fertilization.
  - Extracellular  $Ca^{2+}$  is needed for the acrosome reaction.
  - $Ca^{2+}$  is important in sperm-egg fusion.
  - Intracellular  $Ca^{2+}$  stimulates egg activation.



Yanagimachi, R., & Usui, N. (1974). Calcium dependence of the acrosome reaction and activation of guinea pig spermatozoa. *Experimental Cell Research*, 89(1), 161-174.



Images of a golden hamster spermatozoon penetrating the zona pellucida. Yana's wife, Hiroko, worked alongside him in microscopy. Images provided by Steven Ward, University of Hawai'i at Manoa



Scanning electron micrographs of golden hamster spermatozoa fusing with eggs. Yanagimachi, R. (2009). Germ cell research: a personal perspective. *Biol Reprod*, 80(2), 204-218.

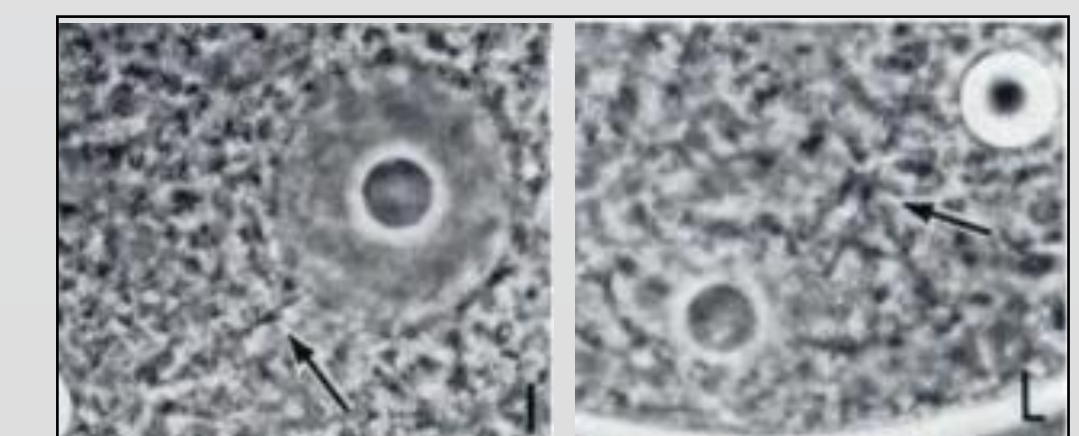
#### The Polyspermy Block

- Yana's laboratory was the first to experimentally show that the changes of the oolemma is important to prevent polyspermy.



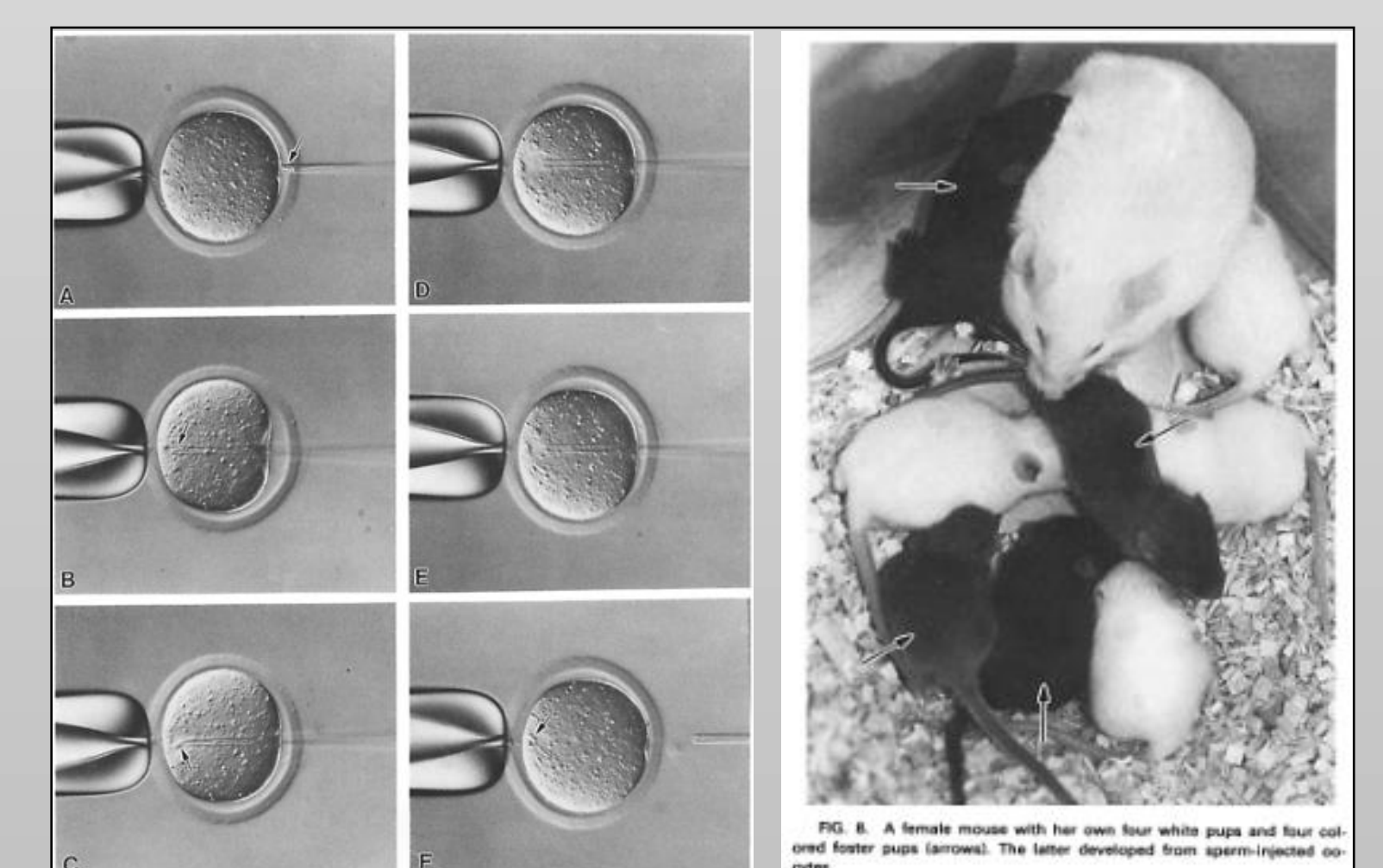
#### Intracytoplasmic Sperm Injections (ICSI)

- In 1976, Yana published a paper in BOR showing how freeze-dried human sperm could develop into pronuclei when injected into a hamster oocyte.
- This was the first mammalian ICSI.



Male pronuclei formed from live (left) or freeze dried (right) human sperm. Uehara T, Yanagimachi R. (1976). Microsurgical injection of spermatozoa into hamster eggs with subsequent transformation of sperm nuclei into male pronuclei. *J Reprod Fert* 15, 467-470.

- The work of ICSI by Yana was shared with clinicians which resulted in the first birth of human babies by ICSI in 1992.
- In 1995, Yana reported in BOR for the first time of mice born by ICSI. Unbelievably, mouse ICSI is more difficult than human ICSI.



Kimura, Y., & Yanagimachi, R. (1995). Intracytoplasmic sperm injection in the mouse. *Biol Reprod*, 52(4), 709-720.

- Yana continued to use the mouse ICSI as a biological assay to test sperm DNA.
- Yana helped to translate benchtop science to clinicians to improve human ICSI for ART.
- Yana's overall goal was to use IVF and ICSI to continue "learning more about the processes and mechanisms of natural (bisexual) reproduction".

#### Overall Contributions to Reproduction

- In this limited space we can not fully highlight all the significant contributions of Yana to reproductive biology and the understanding of fertility. We owe Dr. Yanagimachi a tremendous debt of gratitude.

