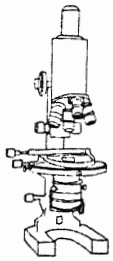

Profile #2
ELIZABETH HAY, M.D.
Professor of Embryology

BIOGRAPHY

Dr. Hay, Chair of the Department of Anatomy, explains how she combines administrative and teaching responsibilities with her laboratory research in developmental biology. A pioneer in the field of electron microscopy, Dr. Hay recalls the excitement of those early years: "Everything I looked at had never been seen before!" Dr. Hay comments on her experiences at Smith College and Johns Hopkins Medical School, and encourages students to seek the new frontiers of science.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Embryologists

Research Scientists — (Ph.D.s) — post-Doctoral Fellows

Ph.D. Students

Laboratory Technicians

Medical Equipment Demonstrated:

Electron Microscope

Positive Flow Hoods for Sterile Tissue Culture Procedures

Tissue Culture Apparatus

Social Concepts Discussed:

The Effects of the Women's Movement on Aspirations and Expectations

The Importance of Collaboration in Scientific Research

The Changes in Government Funding of Research

Being a Pioneer in Your Field

Transcript

Dr. Hay: You asked me about attitudes of other women. I must say this, when I graduated from Smith, I would say the bulk of my friends thought I was really a little crazy to be going to medical school. They all went out and worked for a year or two and their primary goal in life was to get married.

Interviewer: The Joint Committee on the Status of Women in conjunction with the Office for Educational Programs, has produced this series called Women in Medicine to document senior women of Harvard Medical School. Today we're talking with Dr. Elizabeth Hay, Louise Foote Pfeiffer Professor of Embryology and Chair of the Department of Anatomy.

Interviewer: Can you tell us again, briefly, what electron microscopy meant to your career?

Dr. Hay: Well, it was really the starting point of my career. It was a new technique which promised to open up a whole arena of new information about the structure and function of cells and so when Keith Porter and then with his collaborator Palade in the early 1950's showed that the basophilic substance of the cytoplasm consisted of what we then called Palade granules and are now called ribosomes, attached to membranes of the endoplasmic reticulum. This was just an unbelievable discovery that I heard Keith Porter talk about in 1954 at Atlantic City at a Federation meeting. That was when I decided that this was really for me.

So I went back to Hopkins and struggled trying to learn electron microscopy, but it was really hard in those days. Students have it easy now. We didn't have proper embedding materials; we didn't have stains; you were just lucky if you got a good section. That was why I wanted to move to New York, because it was just such an exciting frontier, everything you looked at had never been looked at before. It was just like being the first one to go to the Antarctic, it was a period of just immense excitement.

I did the first electron microscopic analysis of what the cells were doing during regeneration. After we moved to Harvard I did begin to collaborate with John Paul Revel. We developed an autoradiographic technique with the electron microscope using the generating limbs as a model. Then I continued to collaborate with Revel when I began to work on the development of the cornea, which is one of my major interests.

Interviewer: Dr. Hay, could you describe for me your current research interests?

Dr. Hay: Well, I'm interested in tissue interaction in the embryo. I got into it because of my electron microscopic studies, which as I indicated, were on the regenerating limb in the beginning. These studies led me to work on the cornea. The ultrastructural information suggested that the epidermis was playing a very important role in the regeneration of the limb by producing extra-cellular matrix. So I moved into studying the role of the epithelium in development using a cornea as a system in the mid 1960's.

Since then I've been very interested in how extra-cellular matrix produced by the epithelium influences the further differentiation of that epithelium and also influences the differentiation of the fibroblasts that migrate into the sub-epithelial stroma at a later stage of development. In the lab at the present we're trying to dissect out that phenomenon at a cell and molecular level. We're interested in the possibility that all cells have receptors for extracellular matrix and their reaction to extra-cellular matrix varies during development. The real contribution of the work is to call attention to the fact that not only cells but also the matrix that they produce around them during development contains information that leads to the normal embryogenesis. So from the point of view of disease, the difference that this will make in your outlook is that you would not only ask — is there something wrong with the nucleus or the cytoplasm, you would also ask, has the extra cellular matrix been produced properly? At the moment we don't have a list of diseases in which we can point to abnormalities of the matrix as the cause. But I think in the future we will.

Interviewer: How do you actually carry out your research? Do you have a group of graduate students or colleagues with whom you work closely?

Dr. Hay: I have a small group, at the moment, two postdoctoral fellows. Steve Sugrue is working on the epithelium. In his research he has shown that soluble extracellular matrix molecules can affect the basal surface of the epithelium, can cause the cytoskeleton to take on a completely different configuration than it has in the absence of matrix. A second postdoctoral fellow, Jim Tomesac is analyzing the effect of the extra cellular matrix that the epithelium cells secrete on the migrating corneal fibroblasts which invade it. So he is doing studies of isolated corneal fibroblasts and also, at the moment, the cytoskeleton and the effect of extracellular matrix in the cytoskeleton.

My graduate student, Gary Greenberg, is interested in epithelial mesechimal transformations in the embryo and the effect of extracellular matrix on the shape of the cells and in the manner in which they migrate to their environment; and I have two technicians, so it is a small group.

One of the problems as administration increases is staying on the bench. I think it is extremely important for scientists to be on the bench. I do a major part of the electron microscopy on all of the projects that I mentioned to you. Obviously, I love electron microscopy and visualizing what cells are doing. I do most of my own printing of electron micrographs for seminars, lectures and that sort of thing. I make my own slides. I work in the culture room more or less. When I have a new group of people coming in, then I'm at the culture bench setting up the cultures. We have a moderate turnover, the technicians stay about two years if we're lucky and, of course, the postdocs stay about 2-3 years. So that means that there is a constant demand for me to be in the lab. Once a technique for setting up the cultures gets going, it's hard for me to find a seat in the culture room because the technicians and the postdocs are busy setting up the cultures. But, whenever we change a procedure or look for something new, I am there at the bench.

Interviewer: You spent a number of years, also, editing a journal?

Dr. Hay: Yes, the **Journal of Developmental Biology**. I took that on because I was mad at the way they were reproducing electron micrographs. It was a little peanut size journal up until about 1971. So I converted it into a very large-size page and introduced a number of reproductive techniques that they hadn't been using. The only way you could change their attitudes towards publication of electron micrographs, it doesn't do any good to write the editor, you have to be the editor, so that was why I did that.

Interviewer: Dr. Hay, you've recently edited a book on your area of interest. Could you tell me a little about it?

Dr. Hay: Yes. I took on the job because I really feel that extracellular matrix is coming into the forefront and finally cell biologists are realizing that not everything happens within the cell but rather that important things are happening out in the extracellular matrix. In fact, some of our research and the research of others indicates that extracellular matrix is actually telling the cells what to do. I was therefore attracted by the idea of editing a book on cell biology of extracellular matrix when Plenum Press approached me a couple of years ago.

Interviewer: Well, let's go into the issue of you as an Administrative Department Chair. How you divide your time, how you set priorities? You now have to juggle research, teaching, administration and anything else that may come up in terms of being a Department Head. Where do you spend most of your time?

Dr. Hay: Well, I haven't kept track, but I suspect that I spend most of it being Department Chairman, maybe half? I spend perhaps 30% of the time in the lab. It's very hard to say. I certainly spend more time being Department Chairman than any of the other activities that I like to do. I've cut down my teaching, I no longer teach Histology. And I really loved teaching Histology, being in the lab and running lab sections, but it's very time consuming to run a lab section, so I only teach Embryology and Developmental Biology. I teach an intense course in January to the medical students, which is a lecture every day for the month of January. So, except for the developmental biology course I give to graduate students with Joan Ruderman every other year, my teaching load is now relatively light. I had to do that because I had to have time to do my research. Obviously, from what I've told you about my career, the research is the most important part of my life.

Interviewer: Do you see any differences in the young women now studying medicine and your peers?

Dr. Hay: Yes. I think in the last five or ten years the whole attitude toward women has completely changed so that the women coming to medical school today, I think, feel very welcome. For one thing, she's no longer in the minority, she can expect at least 30% of the class to be composed of women. The attitude of fellow students toward each other is certainly different. Although, I don't think Mel Avery and I felt discriminated against, we clearly were kind of in a separate category from the rest of the class. We'll never know what we didn't get to do that the guys were doing.

Interviewer: As Department Chair, you're put in the position of counseling young people. How do you find yourself in that position right now when things for research look so dismal?

Dr. Hay: Well, I really can't believe that the picture can remain this dismal for a significant period of time. We have had downs and ups of this kind over the past 15-20 years and we've bounced back. We haven't bounced back with the kind of research money that we had in the 40's and 50's but we've kept going, and I really would tell any young person today that it's worth getting in there and fighting, I continue to be actively interested in research because I'm sure things are going to get better. Now we may have to wine and dine our congressmen and really pursuade the important people that research is as important as we think it is. I think the fact is undeniable, when you look at what has happened to basic science in the past 15 or 20 years. I couldn't have possibly predicted in my wildest dreams what we would know today. It's been a revolution and it's been because research has been funded by the United States Government. That's not a difficult story to sell a congressman. I really don't think that we'll be out of business. I think research has so much left to discover that we're going to make it. So I encourage young people to go into research.

autoradiography. The making of a graphic record obtained by placing a radioactive material in contact with or in close proximity to a photographic emulsion and developing the exposed film or plate.

basal surface. The bottom or primary layer.

cell receptors. In Ehrlich's theory of immunity, surface molecules of the cell which combine with foreign substances, such as toxins, antibodies, antigens, etc.

cornea. The transparent membrane, forming the anterior sixth of the outer coat of the eyeball.

cytoskeleton. The tonofibrils, keratin, or other filaments serving to act as supportive cytoplasmic elements, especially of certain epithelial cells.

differentiation. Specialization or the acquiring or the possession of character or function different from that of the original type.

electron microscopy. Investigation of minute objects by means of a visual and photographic microscope in which electron beams with wavelengths thousands of times shorter than visible light are utilized in place of light, thereby allowing much greater magnification.

embryogenesis. That phase of prenatal development involved in the establishing of the characteristic configuration of the embryonic body.

embryology. The science of the origin and development of the organism from the fertilization of the ovum to the beginning of extrauterine or extraovular life; in humans, the 2nd to 8th week of life, inclusive.

endoplasmic reticulum. The network of tubules or flattened sacs with or without ribosomes on the surface of their membranes.

epidermis. The outer portion of the skin.

fibroblasts. An elongated cell with cytoplasmic processes present in connective tissue, capable of forming collagen fibers.

histology. The science that deals with the minute structure of cells, tissues, and organs in relation to their function.

sub-epithelial stroma. The framework, usually of connective tissue, beneath the epithelium.

transformations. Metamorphoses; changes of form and shape.

Dr. Elizabeth Hay
General Questions

1. In what ways is Dr. Hay's research a team effort? What procedures does she especially enjoy and largely continue to do herself?

2. What difference does Dr. Hay see in young women now studying medicine and her peers?

3. What does Dr. Hay see as the future for medical research? What advice does she give to those entering the field?

4. What traits of the scientific researcher does Dr. Hay reveal? Why are these traits so important?

5. Given a limited amount of time, what are the potential conflicts that are confronting Dr. Hay as she attempts to deal with her administrative and investigative responsibilities?

6. Dr. Hay is involved with editing the **Journal of Developmental Biology**. Why did she feel compelled to take on this new activity?

7. Dr. Hay was also involved with editing a book on cell biology of the extracellular matrix. What were her reasons for taking on this endeavor?

8. What does Dr. Hay consider to be the most important part of her life?

9. Which would you find more rewarding, a career in research or in clinical work? Why?

Dr. Elizabeth Hay
Science Questions

1. Why was Dr. Hay so excited about electron microscopy in the early stages of her career?

2. What are the current research interests of Dr. Hay? Why did she become involved in this area of specialization?

3. Dr. Hay discusses the significance of the extracellular matrix in normal embryogenesis. What is the relationship between the extracellular matrix and normal embryonic development?

4. The field of biomedical engineering is producing many of the tools used in the diagnosis and treatment of disease, as well as an accumulation of basic knowledge of biological systems. The electron microscope is one of the tools. What are the advantages of this piece of instrumentation? What are the disadvantages?

5. There is a current theory that all cells have receptors for extracellular matrix and their reaction to extracellular matrix varies during development. What is the significance of this newly discovered interrelationship? How is this idea, about factors that influence embryonic development, different from the traditional ideas about control of development?

6. What is another example of molecules secreted by one cell interacting with receptors on other cells and influencing the behavior of these target cells?

7. Why will answers to the basic questions about fetal development be of benefit to people?

8. Suppose a particular molecule was identified as being the primary cause of abnormal tissue development/orientation in the fetus. The molecule in question influences how a group of cells align themselves. This incorrect alignment leads to a specific birth defect. How would this new information, possibly, lead to a treatment of the problem? What might the treatment involve?

Dr. Elizabeth Hay
Social Studies Questions

1. The development of a research team is part of the initial process in pursuing answers to a medical problem. How would you go about forming a team? What personality traits would you look for? What are the positive features of a research team approach to a medical problem?

2. What is it like to be a pioneer in a field as Dr. Hay has been in electron microscopy? Why might being a "pioneer" be especially helpful for women in medicine?

3. Where does much of the funding for basic research come from? What would be the ideal source of financial support? Do you feel this source of funding today is adequate?

4. In the funding for basic research, what is revealed about national priorities? Public awareness? How can individuals influence such policies?

5. Why is the ability to organize time and effort so important to success in research?

6. What ethical issues are raised by Dr. Hay's research, particularly as it applies to fetal development?