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Interview

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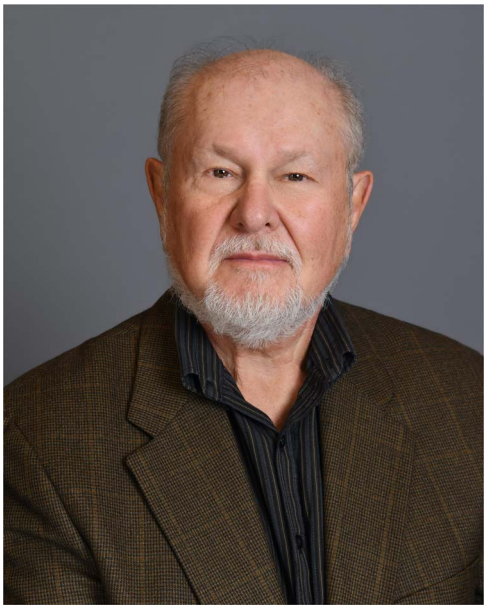
An interview with Dr David Albertini



Dr David Albertini is a Professor of Reproductive Biology at the Bedford Research Foundation, MA. He is also a Visiting Scientist in the Center for Human Reproduction, the Rockefeller University, NY. He received his PhD from Harvard University working under the supervision of legends Dr Everett Anderson and Dr Don Fawcett on the cell biology of the mammalian ovary. After completing his postdoctoral work at the University of Connecticut Health Center, he returned to Harvard Medical School (HMS) as an Assistant Professor of Anatomy and Cell Biology and worked there until 1984. He moved to Tufts University School of Medicine and rose to the ranks of an Associate Professor and Professor and stayed there until 2004. At Tufts, he served as Chair of the Department of Anatomy and Cell Biology (1996–2000), Director of the Center for Reproduction (1999–2003), and Director of the Confocal Microscopy core (1988–1999). From 2004–2016, he held an Endowed Chair as the Hall Professor of Molecular Medicine at the Kansas University Medical Center, Kansas City, KS where he continued his career long interests in reproductive physiology and biomedical imaging, especially as it pertains to the practice of human Assisted Reproductive Technologies (ARTs).

Dr Albertini's major research interests include ovarian physiology and reproductive endocrinology, with a particular focus on oogenesis and embryogenesis, stem cells in reproductive medicine, ovarian cell cytoskeleton, and cell cycle. During his long and distinguished career, Dr Albertini studied oogenesis and ovarian physiology using many species including human. His early work identified the mechanistic basis of meiotic competence, centrosome phosphorylation, and cell cycle dynamics during oogenesis. In early 1990s, he defined the patterns of intercellular connectivity in the mammalian cumulus-oocyte complex, which he later characterized these as transzonal projections and demonstrated their follicle-stimulating hormone (FSH) dependence. Subsequently, in a series of publications, he characterized centrosome sorting, reorganization in vivo, and centrosome-specific perturbations during in vitro maturation of mouse oocytes. Dr Albertini successfully employed many microscopic techniques in his research work. He provided a great deal of ultrastructural analysis on the ovarian and oocyte phenotypes in growth and differentiation factor (*Gdf9*) null mice and characterized oocyte and follicle development in ovaries of these null mice.

Dr Albertini's more recent research work focused on diverse areas including development of methods for oocyte cryopreservation, analysis of oocyte behavior and meiotic spindle dynamics during cryopreservation, identification of germline stem cells and neo-oogenesis in human ovaries, delineation of protein kinases in meiotic maturation, and characterization of oocytes and ovarian outcomes in patients seeking in vitro fertilization. In addition to publishing over 200 peer-reviewed papers, he wrote many thought-provoking reviews and authoritative book chapters. Dr Albertini is an inspiring teacher and colleague. He trained several graduate and postdoctoral fellows, invited many scientists from all over the world to work in his laboratory, and he successfully collaborated with many scientists worldwide. His passion for teaching and training was evident by his dedicated service to the Frontiers in Reproductive Biology (FIR) program both as an Instructor and Course Director.

Dr Albertini received several awards including the 1999 - UK Hammond Medal, Society for Reproduction and Fertility (UK), and 2013 - Beacon Award, Frontiers of Reproduction, Marine Biological Laboratory, Woods Hole. His other academic achievements include recognition as Basil O′ Connor Fellow (1980), Founder's Lecturer of the Australian Society of Reproductive Biology (2001), Colwin Fellow, Marine Biological Laboratory, Woods Hole (2003), and D.H. Barron Lectureship, University of Florida (2016). He has been an invited speaker at numerous symposia and workshops all over the world and he gave more than 250 invited lectures. In addition, he served on the organizing committees of some of the prominent meetings such as Capri Workshops (2013–2018),

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ESHRE Workshops (2014–2017), Foundation for Reproductive Medicine (2016-present), and Ovarian Club, II–XI (2011–2018).

Dr Albertini's vast knowledge of ovarian physiology and reproductive endocrinology led him to often voice his opinion on countless number of occasions particularly, in commenting on latest research in the field published in very high-profile scientific journals, public debates in national and international scientific symposia, and other lectures given to popular media. He also served as a reviewer on many NIH grant review panels and as an ad hoc member of journal editorial boards. Most significantly, he became the Editor-in-Chief (EiC) of *Journal of Assisted Reproduction and Genetics* in 2009 and transformed this journal into a premier scientific journal that reports emerging innovations in human ARTs and mechanisms of human development that bear on the treatment of infertility. A prominent highlight of this journal is Dr Albertini's monthly editorial commentary! These single page editorials are written with exceptional clarity, deep insight into an emerging field, and often loaded with quotations form famous scientists and his typical wit.

Besides well-known for his breadth of scientific knowledge, Dr Albertini is also passionate about sports, particularly, hockey and baseball (Bruins and Red Sox fan), basketball, and college football. While being colleagues during 2004–2016, Dr Albertini and this Interviewer spent on numerous occasions hours at a stretch discussing science, philosophy, evolution, and sports. David, as he is called, has kindly agreed to do this interview for *Biology of Reproduction*.

• What attracted you to biology and animal sciences? and Is ovarian/oocyte biology research pursuit an early passion of yours?

Thanks Raj, an honor and pleasure to share these memories with you. Like so many from my generation, the seeds to becoming a biologist were sown early in a family that encouraged my curiosity about living things-that first microscope and dissecting kit on my 10th birthday got the wheel rolling. And the stream of mentors I was fortunate to have met led me down the path of ovarian biology beginning with Tony Mahowald at Marquette University in whose laboratory I received my first taste of the marvelous oocyte dissecting Drosophila ovarioles. Spending summers during my college years doing research in the Pathobiology Division at the New England Regional Primate Research Center eventually spawned my career long interest in ovarian biology through the chance opportunity to work in the laboratory of a newly arrived investigator known to me at the time as Doctor (emphasis) Arthur Tremain Hertig. My nascent knowledge base of human embryology at that time did not allow me to make the connection between Dr Hertig and the by now famous Carnegie Collection of Human Embryos, made possible by the so-called "egg hunts" of Hertig and Rock from the 1930s and 1940s that took place at the Boston Lying-In Hospital for Women.

Summer and winter breaks from college provided me ample opportunity to work in Dr Hertig's laboratory where I was tasked with conducting "histochemical" studies of ovaries of many primate species whenever a female reproductive tract became available. My very first summer in his laboratory, I would be called into his office to review Hemtoaxylin and Eosin slides of all things female reproductive tract and he must have sensed my curiosity as this became a routine nearly daily practice for a private tutorial-again without me being aware at his career accomplishments and the unique mentoring experience I was having at the time. But as these 3 years progressed (1968–1970), alongside the Viet Nam war and an impending graduation, so did my interest in pursuing a research career in of all things-ovaries! As one of my former PhD students would say: "Imagine Professor, Imagine!"

Dr Hertig, once aware of my interest in graduate school, suggested I apply to several PhD programs in the USA where he knew particular scientists whom he thought would provide a training experience in ovarian biology. In the Fall of 1970, I began graduate school in the Zoology Department at University of Massachusetts (UMass) Amherst and first chance I had I visited Professor Everett Anderson. "Andy"—as he was called—was cordial and invited me to do a rotation in his laboratory noting that I would first have to acquire the basics of electron microscopy before being assigned a specific project given that first year involved mostly course work and being a TA in Zoology. Things moved fast that first year in Amherst and I found myself under the daily tutelage of two lab assistants who guided me into the depths of electron microscopy according to the "Andersonian" tradition. Little did I know, something was brewing that would change the course of my future plans as an "ovary-wannabe-scientist."

• How did you decide to go to HMS and work with the giants Dr Everett Anderson and Dr Don Fawcett to do your PhD thesis work?

As Pasteur said, "Chance visits the mind of the prepared." So, it was that after 6 months, I learned that Professor Anderson and his laboratory would be moving from UMass to HMS to take up residence in the newly formed Laboratory for Human Reproduction and Reproductive Biology (LHRRB). Since Andy's appointment was to be in the Anatomy Department at HMS, I was required to apply to the Division of Medical Sciences and be interviewed by Anatomy Department faculty members, with my exit interview being with Dr Don Fawcett, then department Chair and Founding Director of the LHRRB. Needless to say, the rest is history having matriculated in January of 1972 at HMS and submitting my Master's degree thesis before the move from Amherst to Boston (being a product of the cultural revolution of the 1960s-and having long hair-I admit to being a hippie in practice appearance- Dr Fawcett advised me to get a haircut before showing up in the department).

• What did you work on as a postdoctoral fellow at the University of Connecticut Health Sciences Center?

Membrane biology was the fashion at the time and I was most interested in moving to a different area both topically and technically. I had taken two courses in membrane physiology co-taught by Dick Berlin and Tom Wilson and with Dick moving to become the first Chair of Physiology at the UCONN Health Center, his invitation to join the lab met both objectives of changing fields and moving into a more biochemical and biophysical approach to research. Berlin's lab was truly pushing the envelope to study plasma membrane fluidity using fluorescence spectroscopic techniques, namely fluorescence resonance energy transfer (FRET) and fluorescence depolarization. I worked on two projects. Firstly, I developed FRET for use in microtubule assembly assays that we applied to our studies on microtubule–membrane interactions and the role of reduced glutathione of proton balance in

human leucocytes. Second, we extended my graduate work on cell surface receptor capping to human leucocytes from healthy patients and those suffering from Chediak–Higashi syndrome, a fatal lysosomal storage disease in children under the age of 6. The lab was progressive and opened career opportunities that I could not have anticipated-enriching my background in live cell imaging by fluorescence and opening my eyes to the potential of basic science to contribute to health and well - being- in this case extending the lifespan of children.

• What led you to accept faculty position at the Harvard and then as Chair of the Cell Biology department at the Tufts University?

Unlike today's competitive landscape in seeking faculty positions, 1976–77 was a time of growth and expansion at Medical Schools nationally such that junior faculty positions were available and one could be choosy for that next career step. Betty Hay had become the Chair of Anatomy at HMS during my graduate days and on the day of my thesis defense "welcomed" me back to the Department when "I was ready." So, in the spring of 1977, with seminar and job interview plans in order, I returned to HMS on the designated day only to be handed a schedule that included lunch that very day at the Harvard Club with Dr Fawcett. As they say the rest was history as the details for returning as an Assistant Professor of Anatomy and Cell Biology were easily agreed upon and without surprise, besides my independent research program, I would officially become a gross anatomist. My 6 years at HMS were career defining in many ways and within the first 18 months, I had received 3 grants and built my first lab group with my first PhD student (Scottie Robinson), technician (Nancy Kravitz), and post-doc (Brian Herman). These three people and the platform of camaraderie Betty Hay's leadership generated among the faculty—many of us new hires like Joan Ruderman, Dick Linck, Rich Murphy, Keigi Fujiwara—laid a foundation for my career that I would always cherish. And, to top it off, the birth of my daughters Jenny (1980) and Lauren (1983) enriched the family experience even more as evidenced by their not-so-infrequent visits to the lab on Saturday mornings (does anyone else remember when weekend experiments were the norm not the exception?).

For reasons not worth detailing, the move to Tufts Medical School late in 1984 would be considered a right of passage in those days for academics like myself seeking to remain in the Boston area for the next stage of their career. This opportunity also was realized by a bit of luck and uncanny timing. And retaining my ties to the Boston research community and the many colleagues and collaborators already in place was to be a strong point of departure for the years ahead at Tufts. The road to becoming Chair of Anatomy and Cellular Biology at Tufts was a gradual process, covering a 20-year period. With era appropriate expectations from Tufts University, faculty were conditioned to become "triple threats" meaning that you were expected to excel at teaching, maintain a well-funded research program with graduate students and post-docs, and finally, if you succeeded in this capacity, you would be sought out for administrative work with promotion and tenure hanging in the balance.

That all said, I look back at my Tufts years in awe of the amazing people I had the honor to work with in my lab and who made the family experience fostered by Betty Hay years before become the reality from which I gained immeasurably, and for which I would be forever grateful—thank you Carlos, Britta, Susie, Dineli, Alp, Raquel, Ann, Catherine, Lynda, Mary Jo, Gloria, Liz and so many others Tufts colleagues (Bruce, Ira, the late Steve Adair, John, Eric, Karl) to name just a few of the trail blazers over those years.

• You are very passionate of teaching. What motivated you to decide to spend many hours at the FIR course?

Being passionate about teaching was something I recognized from the earliest days of my graduate education with Andy. It was reinforced and shaped by my colleagues at HMS as I worked to become a gross anatomist and cell biologist with so many mentors who to this day allow me to carry the banner of stimulating curiosity and motivation for all learners (Dan Goodenough, Elio Raviola, and Rich Murphy stand out from those formative years of teaching). When you ask about hours at the FIR course—which I address below—I must admit that experience pales by comparison to the Tufts years where whether Graduate, Dental, Medical, or Veterinary Schools reached out and tap into the resources and energies invested in many courses as lecturer, course director, and curriculum development reformer-duty and service came with a calling to provide students with the mentorship and direction they deserved. As for FIR, yes it was an incredible opportunity to work with remarkable students, melded in context from the basic to clinical sciences, and the people who created this venture at a time when reproductive biology and medicine commanded a nexus that from the past was all too difficult a divide to cross-here too the late Mike McClure, and Joan, the Jerrys (Strauss and Schatten). Acknowledging that one's career trajectory must be judged by the influence of mentors and colleagues who brought depth to their own development and contributions is a sentiment I have carried from my very first mentor Dr Hertig, and was so aptly put by signage in his office with the words: "Appreciation is the sense of favors yet to come." Of all the struggles we face in the altered world of today, I would submit that being unable to recognize and effect appreciation to all our neighbors is a cultural deterrent of today.

• Although you have started your early research career very focused on meiotic cell cycle dynamics, meiotic progression, and centrosome biology, you have broadened your interests into diverse aspects of oocyte/ovarian biology, oogonial stem cells, IVF outcomes, and oocyte cryopreservation. What led you to pursue these diverse areas?

As noted above, I was taught early on in my career to take to heart the Krogh Principle. To paraphrase, for every question one asks in biology, there is an organism ideally suited to provide an answer. As an embryology student at the Woods Hole MBL, we exploited the merits of Krogh's idea in sampling the variety of marine organisms whose reproductive life cycles reveal a panorama of strategies nearly as overwhelming as the choices we have today with data gathering tools—the "Omics" era so to speak.

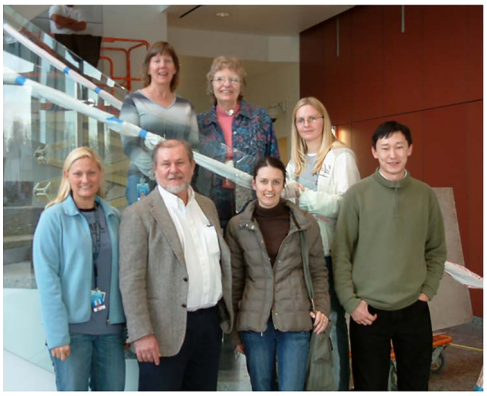
So, it was that I have had the privilege to be flexible and risk taking in choosing the many problems we have worked on over the years (not-so-easy in today's world of funding) because I love to read the literature, engage in conversation, travel to meetings, and now exploit email to reach out and learn more about a topic of potential interest before investing in a more formal study. You note some examples in your Introduction, but eyes wide open was the modus operandi for

why cell cycle control was an obvious direction given my years of experience on an American cancer Society study section and having as an office "neighbor" at HMS Joan Ruderman, she being discoverer of the cyclin family of proteins. Working with primates, whilst we were engaged with mouse knockout work with you and Marty Matzuk, happened because another one of my most valued mentors was John Biggers, with whom I shared one of Tasca's NIH Egg Club grants-work that was facilitated by my long-standing connection with the HMS Primate Center, and that led ultimately to working on oocyte cryopreservation in humans. The final chapter to this particular soiree arose from my Italian colleagues, especially Gio Coticchio, when Italian Law forbade the freezing of human embryos necessitating development of human oocyte cryopreservation from the days of slow-freeze technology to the current standard of care vitrification! In contemporary terms, I see the greatest return now given my shift in direction from animal models to humans and reproductive medicine, this path has serendipitously led to the wonderful world of fertility preservation, a domain that is helping people whose gonadal function has been compromised, and has opened the gateway for research on the human oocyte and embryo. So, what is the take-home message? Keep an open mind, take friendships a step forward when a collaboration brings a piece of your past research into a framework applicable to something not just new but something that could benefit human health first, and add a drop of new knowledge into useful bucket of information that others may share in or use as a point of departure for their own work. Lessons to the wise that may have worked back then, but proceeding through the challenges of an academic career these days may not.

• You are an east coast lover. How did you like your move to the midwest and work at the University of Kansas Medical Center (KUMC) as the Hall Family Endowed Professor?

With deep roots in the east coast, many factors played in to the decision to move to KUMC. For my wife Aline and our children, timing was good as were the Blue Valley Schools given their age and what the future would hold for our family. Family wise, it was a difficult adjustment but in the end, Aline and I felt that the experience was a good one to have gotten out of our provincial New Englandish background and explore life in a different part of the USA. We are grateful for that opportunity and our now adult children have made KC home for them and our newest addition baby Hudson Hotujac, so visits will continue and we are more than happy to switch allegiances from the NE Patriots to the Chiefs (typical of Boston fans and in full recognition of what a great sports town KC is)!

Professionally, I have no misgivings about KUMC and holding the Hall Chair for as long as I did. Bringing you and Lane Chrsitenson into the fold was special for me and my lab and the work we were able to do stands as testimony for another chapter of my career that once again would not have happened without the fantsatic cadre of students and postdocs who shared in the KUMC experience. Special thanks again to Susan Barrett who made the lab transition facile and to Lynda, Karla, John, and of course Darlene Limback who single-handedly carried the Gil Greenwald tradition into the spirit and daily operation of our group. Visiting scientists from around the world got to experience our institution and many collaborations initiated during those years are still alive and well thanks to the generosity of The Hall Family Foundation



and the community of KU scientists we interacted with over the years.

• You have traveled to many countries and established successful collaborations all over the world. How did you achieve these scientific partnerships?

I have alluded to some of these above but at some level I must admit that my training as a teacher was the primary impetus for becoming recognized on an international scale. Yes being one of the few "egg-heads" and ovary aficionados back in the late 1980s and 1990s played a part in why and what a cell biologist saw as the mechanistic and practical challenges working with "wee" cells and "complicated" tissues might garner the attention of both basic scientists and those on the cusp of what would become reproductive medicine. The latter is where the international side of forming partnerships materialized into what has become the second half of my career. How so? With exception to BOR, and my birthright with SSR, as we moved away from mouse work and into human, we tended to publish more in european based journals like HR and RMBOnline. In fact having had several opportunities to get to know Bob Edwards from attending ESHRE meetings and workshops, he asked me to join the RBMOnline editorial Board while I was already on that of Human Reproduction. Since giving a "good" lecture was built into my teaching epigentics, it was natural to bring the lecturing flare to first europe and then the Asian Pacific and Australia. Traveling as an invited speaker, meeting organizer, and doing grant reviewing for various countries converged into something of an addiction, no doubt driven in part by the restless and curious ego that at some level we must all admit to.

• What attracted you to undertake the EiC responsibility of *Journal of Assisted Reproduction and Genetics*?

After some 35+ years at the bench, the JARG EiC position landed on my plate at a time when I was becoming more and more concerned about the divide between basic reproductive biology and clinical medicine especially in the context of human ARTs. Unlike other countries, we in the USA have a dangerous and ever growing admixture of science and politics that has hamstrung federal funding in areas broaching public support for reproductive health, with infertility care managed under the umbrella of but a few medical societies such as the American Society for Reproductive Medicine. The recent Dobbs decision a case in point. Armed with years of Editorial Board experience, and ready to bring a reality check into the publishing realm of reproductive medicine, I took the position

for two reasons. First, here was an opportunity to bring a new generation of basic and clinical scientists into a deeper and more critical evaluation of ART practices that would hopefully rely upon a more scientific basis than currently demonstrable. To wit, one of the accomplishments I am most proud of is building an editorial board for JARG that is not only topically kept up to date (e.g. "omics" specialists) but engages younger scientists and IVF clinicians in achieving the goals of the journal-notably, many board members are former FIR students! Second, as requested during my interviews with ASRM, I wanted a forum that would better disclose weaknesses inherent in study design and push for not only more transparency in data presentation and analysis, but strategically impart "messaging" to all stakeholders in ARTs keeping both safety and efficacy at the top of all publications. Using commentaries, opinion pieces, and other forms of dicourse would become a means to an end. The learning curve has been steep but JARG's goals are being slowly realized.

• In your opinion, where is reproductive biology filed heading to and what is your advice to the current generation of young reproductive biologists?

I am both sympathetic and envious regarding the current generation of reproductive biologists. Sympathetic because the road to traditional academic careers is far more complicated than in my past as are the implicit hurdles to achieve funding burdened further by the "greed" factor of senior scientists outcompeting their own trainees. How and when this might change is unclear. Options exist now for career positions outside the realm of academia and while compromising training in specialties, at least alternatives exist. One example I often encourage new PhDs or posdocs to consider is working in the human ART field as embryologist or lab directors, with the pluses and minuses attendant to this option.

Envious because the world of experimental science offers so much more for getting answers to the many fundamental questions that will comprise a thesis or study destined for publication in a high quality journal. I enjoyed the evolution of imaging and microscopy for nearly four decades and remain awestruck today with the work that is being done on living cells and tissues—whether eggs, follicles, or embryos.

In the end, being fair and honest with your competitors and staying curious are both gifts to offer to colleagues that in the best of worlds will reap personal and professional benfits conducive to your contribution to society.

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