THE ENDOMETRIOSIS ASSOCIATION OPENS A NEW CHAPTER IN RESEARCH PROGRAM AT VANDERBILT
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Since 1999, the Endometriosis Association has partnered with Vanderbilt University School of Medicine to fund and coordinate a “dream team” of scientists to research endometriosis (endo). The program has been highly successful, resulting in truly excellent research that has helped move our scientific understanding of endo forward at a fast clip.

A second contract was recently completed to continue the partnership for seven more years. To celebrate this benchmark, Vanderbilt hosted a gala, a scientific presentation for other scientists at Vanderbilt, a reception for Vanderbilt dignitaries and members of the Endometriosis Association, and a community educational event.

The Endometriosis Association’s partnership with Vanderbilt is unique in the world of science. Never before has a major medical institution made such a bold commitment to true partnership with a nonprofit — that is, Endometriosis Association members, via the headquarters staff, constantly feed information about the experience of endo to the team, who then coordinates it with scientific thought.

That powerful combination has made a huge difference and greatly encourages the scientists. Too often scientists work in a vacuum without knowing how their work actually makes a difference for people. The Endometriosis Association has taken many steps to make sure that Vanderbilt scientists understand the major difference they make. As Kevin Osteen, Ph.D., the visionary Director of the Endometriosis Association Research Program at Vanderbilt University School of Medicine, attribute this to the leverage they can create with the Endometriosis Association’s support. Osteen is the primary investigator for three NIH grants: one examining progesterone failure in the endometrium of patients with endo; another examines the relationship between endo and the failure of a protective anti-inflammatory protein; a third studies the relationship between environmental toxins, particularly dioxins, and endo. Bruner-Tran is the primary investigator for an NIH study to develop a new model of experimental endo that will allow a closer examination of the role of the immune system in the development of endo. Truly, as a recent article in a Vanderbilt publication states, the work has been “highly influential for today’s emerging understanding of endometriosis.”

The new understanding of endo, based on many scientific discoveries over the last ten years, paints a picture of a far more complex disease than ever imagined when the Endometriosis Association started twenty-nine years ago. This has increased the excitement among researchers worldwide. Now, if funding can match that excitement, we will perhaps be able to break through to a complete picture of the disease that should open the door to much better treatments and perhaps even a cure and prevention.

At the same time, the team has not forgotten the clinical aspects of the disease. As Esther Eisenberg, M.D., Professor of Obstetrics and Gynecology, and a key member of the Vanderbilt endometriosis team, states, “in harsh cases, on a scale from 1 to 10, the pain is 15.” It was Dr. Eisenberg who adopted a new treatment in her clinical practice in recent years. For patients with intractable pelvic pain, she uses a combination of fish oil and progesterone. As Dr. Eisenberg has noted, even in patients who have come in on high levels of narcotics, this approach has helped. It seems to counteract some of the inflammation that may cause pain and, as the research in the lab shows, the fish oil may even help dampen the impact of dioxin exposure.

Osteen and Bruner-Tran shared information on this new clinical research at a panel the Endometriosis Association presented in San Francisco last year. (This was reported on in the Endometriosis Association’s Volume 27, No. 5-6 newsletter.)

In addition, the Vanderbilt team’s work has helped lead to potential new treatments. “The core mechanisms of the disease and the potential therapeutic targets are beginning to be revealed,” said Osteen. Our lab has taken a lead in helping pharmaceutical companies identify potential therapies. . . .”

One of the requirements in the Endometriosis Association’s contract with Vanderbilt is that the team will always include an international scientist, typically at the junior level when scientists travel for additional training. The newest international fellow is Tianbing Ding, Ph.D.

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There are still many questions facing scientists about endo. The Vanderbilt team has noted the following that they find particularly intriguing.

- “Is the immunological dimension of endometriosis a cause or a result of the disease?”
- How might inflammation promote endometriosis, and what is the association with other inflammatory processes in the pelvic theater, such as that leading to irritable bowel?
- How does progesterone inhibit inflammation?
- What’s the significance of the association between endometriosis and increased exposure to certain environmental toxins?
- What underlies the association of ovarian cancer and endometriosis in the ovary?
- In what sense is endometriosis an inherited disease?
- By way of strengthening anti-inflammatory mechanisms, how effective could nutrition be in inhibiting endometriosis?
- Could more powerful, synthetic versions of progesterone stop endometriosis?”

“The broad scope of these questions explains why people once typically gave up on finding a cure,” Osteen has said. But as members and donors involved with the Endometriosis Association will agree, we will not give up! With the support and vision of this “dream team” we can find even more answers!


KEY FINDINGS FROM VANDERBILT ENDOMETRIOSIS ASSOCIATION RESEARCH

- Demonstrated a critical role of retinoic acid, the bioactive form of Vitamin A, in controlling normal endometrial expression of matrix degrading enzymes
- Found that a loss of progesterone sensitivity is a central component of the pathophysiology of endometriosis
- Identified that in utero and developmental dioxin exposure in mice creates the same endometrial phenotype observed in women with endometriosis. (Recognized by the European Teratology Society as the best Reproductive Toxicology paper of 2007)
- Discovered an epigenetic link between dioxin action and the loss of progesterone response observed in women with endometriosis
- Presented evidence that dioxin exposure leads to an altered pathway of cell-cell communication in the endometrium that mimics an inflammatory-like event
- Discovered developmental exposure of mice to dioxin leads to disruption of endometrial function for multiple generations, suggesting this toxicant can impact endometrial biology thru the germline
- Demonstrated that nutritional anti-inflammatory agents such as fish oil can provide some protection against the disruptive impact of dioxin on endometrial function
- Developed a novel model system in which the role of immune cells can be examined in the development, progression, and therapeutic treatment of endometriosis
- Developed a unique model of surgical adhesions that allows the role of inflammation to be examined during the earliest stages of endometriosis-mediated adhesion development
- In collaboration with multiple pharmaceutical companies and other NIH-funded investigators, continue to screen new compounds for potential use as therapeutics for women with endometriosis
TRACY H. DICKINSON EPIGENETICS RESEARCH LABORATORY

The Endometriosis Association Research Program at Vanderbilt University School of Medicine has led the way in understanding the impact of embryonic* exposure to dioxins. The horrific findings are clear: exposure to dioxins in the womb during the early part of pregnancy is toxic, and that toxicity extends into many generations in the future. This work has helped explain why we are now seeing so many families with endometriosis across generations, and it also makes it clear how important this research and potential preventative efforts are! Because of the importance of this research and to honor Endometriosis Association board member and longtime donor Tracy H. Dickinson, the Endometriosis Association has named a new research laboratory at Vanderbilt “The Tracy H. Dickinson Epigenetics Research Laboratory.”

More and more, science is understanding that the “programming” of the embryo impacts that individual’s functioning for life. This programming can be impacted by the toxins in the mother’s body (and also toxins the father was exposed to in at least two months before conception), nutrition, stress, et cetera. There is now data to support a link between early exposures in the uterus and obesity, heart disease, and cancer in addition to endometriosis. Therefore, the Endometriosis Association’s continuing work in this area will have benefits across many areas of human and animal health.

Here is how the Endometriosis Association’s Vanderbilt team describes some of their recent work in epigenetics: “We have recently demonstrated adult endometrial dysfunction in mice following developmental [in the uterus during organ development] exposure to TCDD** [dioxin]. Endometrial changes were markedly similar to alterations observed in the endometrium of women with endometriosis, and it resulted in reduced progesterone responsiveness and infertility. . . . It behooves us to determine if children exposed at early developmental timepoints demonstrate an increased sensitivity to additional adult toxicant exposures and whether repeat exposures are necessary for the development of adult diseases such as endometriosis.”

The Vanderbilt team continues: “The Tracy H. Dickinson Epigenetics Research Laboratory will have a strong focus on examining the potential role of epigenetic alterations in endometriosis-associated endometrial dysfunction. Epigenetics refers to hereditable changes to an individual’s genetic make-up, and numerous environmental factors (including TCDD) have been found to be epigenetic modifiers. Importantly, TCDD can activate an inflammation-like cascade, potentially amplifying the risk of epigenetic modification. Our data has pointed to the influence of local inflammation in the loss of progesterone sensitivity observed in the uteruses of women with endometriosis.”

Thank you to Tracy H. Dickinson for making this important work possible! Many other donors also contribute to the Endometriosis Association’s work at Vanderbilt and other research programs, including the Harry & Betty Quadracci family. We and those affected by endometriosis appreciate all our donors!

* Embryonic: in early pregnancy, the embryo is laying down the very beginnings of what will become organs and other major functional expression in the future.

**TCDD: dioxins, specifically, 2,3,7,8-tetrachlorodibenzo-p-dioxin — the most toxic of all the dioxins. For more information, see the Endometriosis Association’s book, The Endometriosis Sourcebook. Order it online or from the Endometriosis Association headquarters.