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## MISSION:

*To encourage scientific research toward finding the cause of and cure for the fibromyalgia syndrome (FMS) as well as to promote public awareness and understanding of this condition.*

*To support educational, scientific and charitable activities undertaken exclusively in connection with FMS and related disorders.*

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# UPDATE

Organizational News and Activities

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## 22<sup>nd</sup> Project Funded - *In Memory of Laura Skalla*

**Award Amount:** \$28,049 - January 2002

**Title:** EBV Transformation for Genetic Studies on FMS

*(Tag-on to a larger genetic study involving 400 subjects)*

**Principal Investigator:** Laurence Bradley, Ph.D.  
University of Alabama at Birmingham (UAB)

In the last issue of the Update (August 2001), we mentioned that AFSA was in the process of approving a research project that would be awarded in memory of **Laura Skalla**, an FMS patient who died tragically in an automobile accident last year. What follows is a description of the award that we alluded to in the last Update. Unlike most projects that are funded in the biomedical field, this particular AFSA study will lay the groundwork for an unlimited number of future genetic studies on FMS. In simple terms, the "EBV transformation" in the title above is a process that takes blood samples and immortalizes the genetic material in the cells to generate a replenishable supply of DNA that can be used for qualified AFSA applicants at anytime well into the future. The usefulness of this project will span many years and, in like fashion, we hope that this facet of the study helps to preserve the memory of Laura for the hundreds who contributed on her behalf.

Evidence for a sex-dependent genetic predisposition for the development of FMS is slowly accumulating. The first published study in the 1980s by **Mark Pellegrino, M.D.**, hinted that the genetic predisposition of FMS may be strong, but that the expression of the condition was more likely to occur in female offspring. Many studies since have implicated a strong genetic role in FMS, including studies showing the high incidence of FMS-like sleep disturbances in school-aged children of mothers with FMS, and a genetic abnormality pertaining to the way the nervous system in FMS patients regulates the production of serotonin ... an important transmitter involved in pain and sleep.

**Laurence Bradley, Ph.D.**, and his team of FMS experts at UAB plan to compare several measures of pain sensitivity, blood serum serotonin levels, and the frequency of a specific polymorphism in the promoter region of the serotonin transporter gene (5-HTT) in eight (8) groups of subjects. This will build on recently published genetic findings on polymorphism of 5-HTT in FMS patients (polymorphism means more than one structural abnormality occurring in the gene, and in this case, the gene that regulates serotonin production). The eight groups of subjects are: 80 female FMS probands, 80 sex-matched control subjects, 40 sisters and 40 brothers of the FMS probands, 40 sisters and 40 brothers of the control subjects, 40 male spouses/partners of the probands, and 40 male spouses/partners of the controls. These procedures will be performed over a 5-year period as the core part of a larger genetic study.

Bradley anticipates a rank ordering of pain sensitivity across the eight subject groups with the

*Continued on page 2*

## Life's Uncertainties Abound, but NOT the Need for FMS Research

Unrest and turmoil exist around the world. Yet, the need for biomedical research on common conditions, such as FMS, permeates the boundaries of countries and cultures. FMS is everywhere you turn and the only way to minimize its path of destruction is through stepping up research on the disease. This is AFSA's mission, and it is due to your generous donations that our research funding goals can be met. Each year brings with it new challenges, and each year we depend upon your help.

## YOUR FMS LEGACY

Ordinarily, a legacy is something that you are proud to leave behind for the younger members of your family and the next generation that is yet to be born. But there is nothing to rejoice about in the case of FMS genetic predisposition. The situation doesn't have to be so grim. Mold your legacy into a person of action, one who changes the direction of FMS research. The genetic study described is just a start. AFSA plans to build upon this project of generating replenishable DNA by getting genetic-minded researchers to submit grant proposals that will lead the way to a better understanding of FMS as well as more effective treatments. This strategy is only a segment of our future funding plan. It will cost money, but with millions of Americans fully understanding the detrimental impact of FMS, this task *is* doable. Become a part of the plan for the future ... and that of generations to come. Contribute to AFSA and change the face of *your* FMS legacy today.

greatest pain sensitivity among the FMS probands, followed by their sisters, followed by their brothers, and then among the remaining groups (controls, sisters and brothers of the controls, and the two spouse/partner groups). He anticipates similar relationships among these subject groups and serum serotonin levels. It is also believed that serum serotonin levels will be found to make a significant contribution to the group differences in pain sensitivity. Finally, the UAB team suspects that the polymorphism in 5-HTT will be found significantly more frequently in the FMS probands compared to the controls. Exploratory analyses will be performed to determine if the polymorphism is found more frequently in the sisters of the FMS probands compared to all of the other sibling groups.

Support from AFSA will allow UAB to create a replenishable supply of genomic DNA from the blood serum donated by the participants using a procedure called EBV transformation. This will ensure that Bradley's team has a sufficient supply of DNA to test their hypotheses concerning the 5-HTT polymorphism. It will also allow them to perform future genetic studies regarding the causes of abnormal pain sensitivity among women with FMS as other candidate genes are identified by basic science investigators. In other words, new findings produced in basic science studies will lead to additional genetic projects using the human DNA material collected by Bradley's team. Moreover, genetic DNA material from human subjects who provide consent will be kept in frozen storage to be made available to other qualified investigators with promising research ideas concerning the causes of FMS. Long delays to recruit 400 samples and the corresponding massive amount of clinical data on each sample will be circumvented by the AFSA project. As Bradley explains in his grant proposal, it will take five years to collect the samples and data, but once the project is completed, future investigators can swiftly obtain the genetic material at a very minimal cost of shipping and handling!

"This project will contribute to more rapid advances in our understanding of the causes of abnormal pain sensitivity in

women with FMS, and thus may lead to significant advances in treatment," says Bradley. The genetic glitches that are the most substantial can be targets for early therapy. Currently, there are so many abnormalities in FMS that it is difficult, if not impossible, to know which ones appear first, and then cause other abnormalities to develop. Genetic studies will greatly clarify this confusion. As science progresses, there is also the hope that genetic knowledge can lead to genetically-based treatments. Summing up the significance of this AFSA-funded project, medical advisor **Robert Bennett, M.D.**, says, "This project will hopefully establish AFSA as a 'major player' in FMS research."

END

## Cytokine Abnormalities Official! AFSA-Funded Study Appears in *Rheumatology*

The July 2001 issue of *Rheumatology*, featured an AFSA-funded project by UCLA professor **Daniel Wallace, M.D.**, and his coworkers titled: "*Cytokines play an aetiopathogenetic role in fibromyalgia - a hypothesis and pilot study.*" The report not only showed that cytokine chemical abnormalities were substantial, but it also provided a basis for how FMS may progress over time. In addition, the study lays the groundwork and justification for investigating the use of two classes of novel pain relievers; one of which has just been approved by the FDA for prescription sale.

Cytokines are produced by the immune system and can cause many—if not all—of the symptoms of FMS. Wallace looked for cytokine abnormalities in FMS patients, and he added to the scientific intrigue by subdividing the FMS patients into "early stage" (symptoms for less than two years) and "late stage" (symptoms for greater than two years). Why evaluate the two groups separately? Wallace cites studies indicating that when FMS is diagnosed and treated in the early stage,

remission of symptoms is likely to occur. But, once the symptoms have persisted for over two years, remissions are rare. So the study intent was not just to look for cytokine abnormalities, but to also investigate a plausible basis for why remissions rarely occur once FMS has persisted for a number of years (i.e., the typical patient).

Before addressing Wallace's major findings, it should be noted that cytokines are not easy substances to analyze. They are released by cells throughout the body and rapidly disappear into the blood circulation. To overcome this obstacle, Wallace not only looked at cytokines and their receptors in the serum, but he assayed for the ability of the patient's blood cells to produce cytokines when stimulated by such substances as LPS, which can resemble a bacterial invasion. Naturally, a control group of healthy people was also included in the study for comparison.

Serum levels of Interleukin-1 receptor antibody (IL-1Ra) were significantly higher in both patient groups compared to con-

# AFSA MEMBERSHIP CONTRIBUTION FORM

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*(see back cover for more info)*

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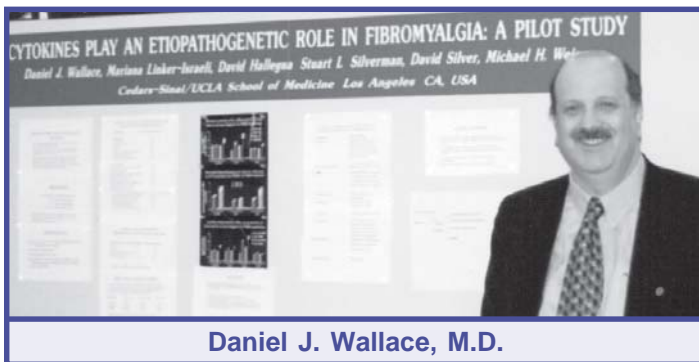
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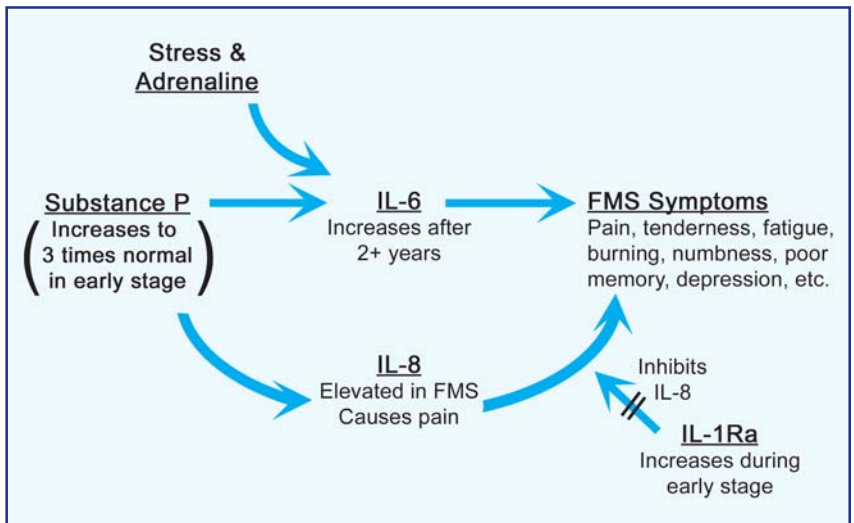
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**Daniel J. Wallace, M.D.**

remissions rare) after several years of persistent symptoms. Cytokine interactions with the body's pain, hormonal and stress response mechanisms are complex. The diagram below helps explain the relationships along with the study findings. Wallace indicates in his report that over time, the level of response to stressors may increase the production of IL-6, but the protective dampening mechanisms provided by IL-1Ra may be exhausted or overwhelmed. Fortunately, a drug that acts like IL-1Ra has just been FDA approved, with many more cytokine-altering drugs soon to be released. There is hope that these abnormalities and the symptoms that they produce can be minimized in the near future. **END**

trols. In other words, the level of IL-1Ra did not appear to be influenced by the duration of FMS symptoms. Plasma levels of Interleukin-8 (IL-8) were three times higher in patients (almost predominantly due to those in the late stage of FMS). Interleukin-6 (IL-6) levels were not elevated in the sera of either FMS group, but when stimulated, IL-6 was produced in substantially higher quantities in the late stage patients, compared to those with early stage FMS and the controls. The stimulated production of IL-1Ra was also higher in the late stage group. In a nutshell, there are significant changes in cytokine production even in the early stage of FMS, but this production generally increases as the duration of symptoms progresses. This latter finding could explain why symptoms tend to worsen with time and why therapies are often less effective (and



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## Marathon Fundraiser

Doug Pacht's best friend's mother, **Claire Cohen**, suffered miserably with FMS and died of causes unrelated to FMS a year ago. The fact that Doug knew a person with FMS is not at all unusual. FMS is a highly prevalent condition; roughly 3-5% of the population has it. The novelty of Doug's story is that he went through a tremendous amount of effort to help people with FMS, even though he did not have the condition himself. After Claire passed away, Doug sought out possible ways to sponsor research in FMS.

A resident of Florida and an avid runner, Doug entered himself into the New York City marathon race that occurred last November. Before the race, he did his homework to find out which charitable organization was most active in funding research on FMS ... that's when he came across the AFSA Web site. He contacted AFSA about his plan to solicit sponsorships for running the marathon race in Claire's honor and donate all the money to AFSA on her behalf. After all the pledges were made (totaling \$955 due to his wonderful fund-raising efforts), Doug still had to run 26 miles for people with FMS **and** collect the money to mail in to AFSA.

Doug's enormous effort, made on behalf of FMS patients everywhere, is proof that there are people who genuinely care about your well-being! **END**

## Cost-saving Disclosure:

Visit our Web site at [www.afsafund.org](http://www.afsafund.org) for all scientific abstracts and info pertaining to AFSA-funded projects. The financials for each year are disclosed on the site as well, so you can see that over 90% of your donations go to research. Also, if you are interested in purchasing the "**AFSA 2000 Syllabus & Speaker Transcripts**," details of this 140-page bound publication can be found on our Web site. It's a great educational tool, while at the same time, it helps AFSA raise funds for more research.

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