2014 Impact Statement

for Prader-Willi Research

FOUNDATION FOR
PRADER-WILLI
RESEARCH
Working Toward an Independent Future

OUR FOUNDATION

The mission of FPWR is to eliminate the challenges of Prader-Willi syndrome through the advancement of research.

FPWR is dedicated to fostering and supporting research that will advance the understanding and treatment of PWS.

To date, FPWR has invested over $4,500,000 in funding to leading scientists and research laboratories around the world.

2014 Summary

In 2014, FPWR supported
20 cutting edge projects and initiatives.

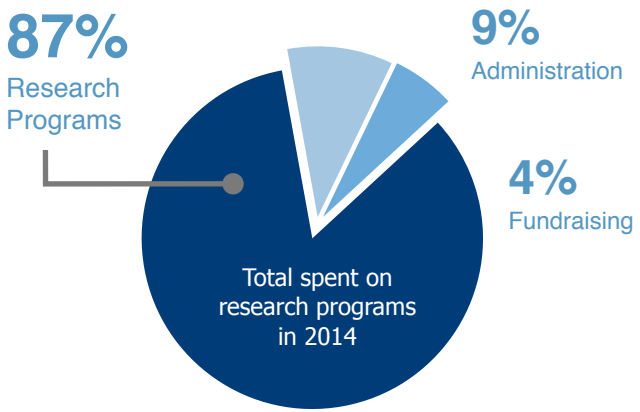
FPWR **awarded over $1.2 Million** to accelerate high-impact PWS research.

Findings from FPWR funded studies were published in
23 scientific publications.

Maximizing Your Investment

FPWR maximizes donor contributions. In 2014, 87% of every donation was used to directly fund research programs. In partnership with the NIH, academic institutions and private pharmaceutical companies, FPWR ensures that your dollars are used to effectively accelerate research and advance potential therapies to treat the many challenges of PWS.

Functional Expenses



FPWR GRANTS PROGRAM

FPWR manages a robust grants program inviting PWS experts from around the world to submit their best ideas for review. Among the general grant applications are project proposals addressing the basic science of PWS; studies whose aims are to better understand the underlying mechanism by which disruption of PWS-region genes leads to the characteristics of PWS. New approaches to therapies are also tested in many of these proposals, allowing “go/no go” decisions to be made on treatment options, and laying the groundwork for full clinical development.

2014 Funded Research

Discovery Science

- Autism in PWS
- Gene expression
- Behavior task switching
- Brain Imaging
- Gene therapy
- Drug screening
- Gut Microbiome
- Metabalomics
- Hypotonia

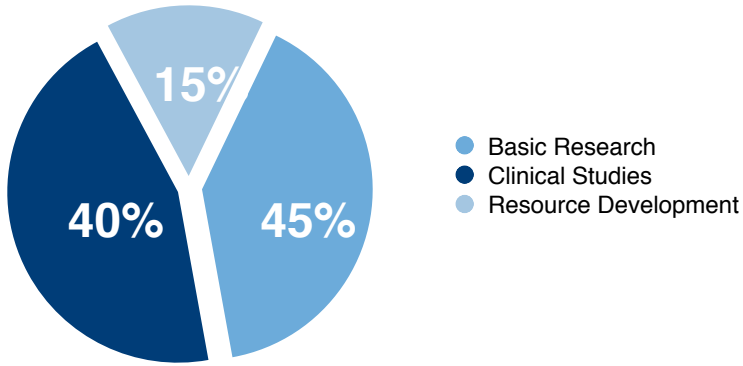
Resource Development

- Global PWS Registry
- New Magel2 PWS Rat Model
- New SNORD116 PWS Rat Model

New Clinical Trials

- Diazoxide for hyperphagia
- Transcranial DCS for hyperphagia
- Sulfamethoxazole for hypotonia

Research Profile



PWS CLINICAL TRIALS

Recently developed drugs present promising new opportunities for the treatment of PWS. Many drugs currently in development have potential to greatly improve aspects of PWS. We have identified a list of candidate drugs for PWS that could help with obesity, behavior and overall health.

With conservative estimates suggesting a minimum of $1,000,000 needed to investigate each drug, funding needs for clinical trials are vast. FPWR is working with academic institutions, companies in the pharmaceutical industry and the NIH to leverage our resources and advance trials on candidate drugs as quickly as possible.

2014 IMPACT

- FPWR facilitated three new clinical trials to test novel therapeutics for PWS. Preliminary results from these trials are expected in 2015.
- FPWR investigators Dr. Bouret and Dr. Stuber have advanced the understanding of the normal brain circuits that control hunger and satiety. They are currently investigating how these circuits are disrupted in animal models of PWS.
- FPWR has developed key resources (new mouse models, cellular models, bioinformatics) which have been adopted throughout the scientific community – these resources are critical for efficiently advancing future investigations.
- FPWR investigator, Dr. Liebel (Columbia University), produced the world's first human hypothalamic neurons in a dish which will allow for a deeper understanding of these critical brain neurons. This breakthrough will allow Dr. Leibel's lab to directly examine the function of these neurons in comparison to those from individuals with PWS and will provide critical insights into why the hypothalamus doesn't function appropriately in PWS.
- FPWR mobilized collaborative relationships with pharma, key advocacy groups, academia, regulatory agencies, other non-profit organizations, and patients/caretakers in the PWS community to accelerate clinical trials.

GENE THERAPY

All individuals with PWS have the PWS region genes present, but inactive. FPWR is funding research to explore gene activation and gene therapy methods to potentially change the clinical outcomes of PWS by:

1) Activating genes in the PWS region and/or

2) Replacing the functionality of single PWS genes, such as the MAGEL2 or SNORD116.

Genetic studies like these will provide a better understanding of the genetics of PWS and may lead to new treatments for PWS.

Next In 2015…

- Characterize the newly developed PWS models to better facilitate investigations requiring animal models.
- Launch the Global PWS Registry, which will be used to collect patient data to better understand the PWS phenotype, look for trends, perform statistical analysis and facilitate clinical trial recruitment.
- Build upon our successful grants program to support the best research ideas in the world with particular focus on defining the underlying genetic deficit, understanding disrupted brain circuits and exploring novel therapeutic approaches.
- Continue partnering with pharmaceutical companies to advance therapies for PWS.
- Implement recommendations from the PWS Mental Health Workshop, held March 2015, including support for new mental health initiatives.

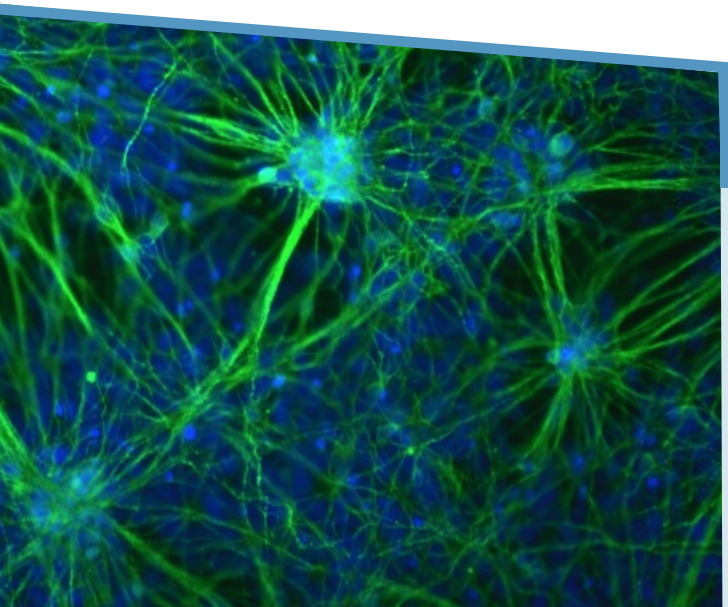
A single gene, MAGEL2, which resides in the PWS region, was recently implicated as potentially underlying some of the major features of PWS. If the MAGEL2 function can be replaced, we may be able to change the clinical outcome of PWS.

Thanks to a generous contribution, FPWR has created two new rat models of PWS that are missing the MAGEL2 and SNORD116 genes. The full characterization of these models in 2015 will allow us to screen existing drugs and test for efficacy in replacing the gene function.

Highlighted Accomplishments

In 2014 alone, FPWR invested over $1.2 Million in Prader-Willi Research. Over the past 12 years, **FPWR has supported nearly 100 high-quality research projects** at top medical and research institutions around the world. At the heart of our research program is **scientific collaboration** which is encouraged through scientific workshops and meetings, resource development and resource sharing grants. Below are just a few of our accomplishments to date.

- FPWR has committed more than $4.5 million in PWS research, supporting projects ranging from basic science to clinical studies, and covering a variety of fields including genetics, obesity, neuroscience, model systems, behavioral research and therapeutics development and evaluation.
- FPWR supported projects have generated more than 70 publications in the medical literature to date, including publications in Nature Neuroscience, Journal of Clinical Investigation, Proceedings of the National Academy of Sciences, Molecular Cell, and Human Molecular Genetics.
- FPWR funded investigators have received more than $6 million in additional support from NIH and other government granting agencies to continue/expand studies started with FPWR funds.
- The Global PWS Registry has been developed by FPWR and will launch in 2015. The Registry will provide a secure platform in which to aggregate clinical data, facilitate the completion of clinical trials, and guide the development of standards of care.
- FPWR has drawn new scientists into the PWS field, helping to launch several investigators in independent research careers.
- We have developed the One SMALL Step global fundraising effort for PWS research, which raised over $1.5 million through walks around the globe in 2014.
- FPWR has supported scientific workshops and meetings to prioritize research [Resnick, 2013] and build consensus on clinical issues [Deal, 2013].
- FPWR supported projects have led to the development of key resources for use across the scientific community (new mouse models of PWS, the generation of induced pluripotent stem cell models; bioinformatics).
- We are supported by a strong global patient community; with over 1,000 members and a reach of more than 6,000 on social media outlets.



Resource Development

FPWR recognizes that supplying researchers with the tools to conduct their studies is critical for accelerating progress, and thus we have invested in the development of several models of PWS. FPWR supported the creation of the first **induced pluripotent stem (iPS) cells** (seen to the left), which will allow us to determine how PWS cells are different from typical cells. These cells will also provide a platform to test small molecules, existing drugs, new drugs, genes, etc as potential therapeutics. Most recently, FPWR funded the development of two rat models, each with a disruption of a critical gene in the PWS region. The full characterization of these new rat models and their use in drug development promises to bring a host of new opportunities to understand and treat PWS.