The Center for Research in FOP & Related Disorders Update

Frederick S. Kaplan, MD, Robert J. Pignolo, MD, PhD, Eileen M. Shore, PhD

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Since it was established in 1991, the Fibrodysplasia Ossificans Progressiva (FOP) Collaborative Research Project at The Center for Research in FOP& Related Disorders has had a singular mission—to determine the cause of FOP and to use that knowledge to advance the treatment and a cure for FOP. During the past twenty-five years, we moved from the wastelands of a rare disease to the watershed of clinical trials. We identified the genetic cause of FOP and used that knowledge to spearhead worldwide research efforts to develop therapies that will transform the care of individuals with FOP.

In partnership with our benefactors, we have expanded the frontiers of discovery and drug development in this rare and catastrophically disabling condition, dismantled the physical and perceptual barriers that have impeded progress, and inspired global research in small molecules, antibodies, and gene therapy for FOP. The Center for Research in FOP & Related Disorders has provided the infrastructure of flexibility and intellectual space needed for serendipity and continuity.

Here, at The Center for Research in FOP & Related Disorders, our work is broad and comprehensive while focused on seven spheres of FOP activity: Clinical Care and Consultation Worldwide, Clinical Research and Infrastructure Development, Basic Research (Identification of Therapeutic Targets), Translational Research (Preclinical Drug Testing & Biomarker Discovery Program), Developmental Grants Program, Clinical Trial Development and Proof-of-Principle Investigation in Patients, Education.

The Center for Research in FOP & Related Disorders is unique. It is the world's first and only comprehensive program in FOP. Here at The Center, we have had a very busy year, and have achieved many milestones. Clinically, The Center directs the world's largest FOP clinic and referral center here in Philadelphia, while conducting international FOP clinics in Italy, Serbia, England, Germany, and Russia.

In clinical research The Center has completed a global surgery survey of FOP flare-ups and designed and validated the FOP Cumulative Analogue Joint Involvement Scale (CAJIS). Clinical trials have also commenced with Palovarotene, an inhibitor of endochondral bone formation, in adult FOP patients. This represents the first randomized double-blind placebo-controlled trial in the history of FOP and was developed with Clementia Pharmaceuticals and the FDA

At the benchtop The Center has made great strides in elucidating the molecular mechanisms by which FOP flare-ups occur and have identified potential therapeutic targets for the treatment of FOP. Additionally, The Center has completed the second-year of a comprehensive pre-clinical drug-testing and biomarker discovery program in FOP mouse models. In this program, a promising compound was discovered that partially inhibits heterotopic compound that partially inhibits heterotopic ossification in a mouse model of FOP. Ongoing studies, both *In vivo,* and *In vitro* are also looking at other potential therapeutic compounds. For this promising work The Center was awarded a new 2-year developmental grant on induced pluripotent stem cell modeling for FOP.

Our work at **The Center** is at the forefront of the FOP world. The work is constantly evolving as we cross the bridge daily between the clinic and the laboratory and back again in a process that builds knowledge and deep understanding to help us accomplish our mission.