Perelman School of Medicine
University of Pennsylvania

Eileen M. Shore, Ph.D.

Report to Dr. Roberto Bufo and the Italian POHA – December 2015

Research investigations dedicated to finding the cause and establishing a cure for POH are conducted at the University of Pennsylvania School of Medicine (Philadelphia, PA, USA) with the support of the Progressive Osseous Heteroplasia Association. Initial investigations to understand POH were noted with the first report of POH as a distinct clinical disorder of heterotopic ossification in 1994. In 1996, the first POHA grant was awarded to study the molecular basis of POH. In 2002, we reported our discovery of the mutation that causes POH in the *GNAS* gene.

Studies supported in part by the Italian POHA are:
1. Evaluation of the DNA sequence of the *GNAS* gene in patients who have received a clinical diagnosis of POH. These studies investigate the correlation between clinical presentation and specific gene mutations as well as increase our understanding of the range of mutations that cause POH.
2. Investigations of the role of the *GNAS* gene in directing the differentiation of cells. Understanding the cellular origins and molecular pathways in bone formation that are controlled by *GNAS* gene products will help us develop treatments for patients with POH and also for more common diseases of bone formation. We are investigating the signaling pathways downstream from *GNAS* that regulate osteogenesis in order to identify therapeutic targets.
3. We are examining the effects of *GNAS* gene mutations on skeletal bone structure and quality in order to evaluate the impact of these mutations on the bone health of the normal skeletal in people with POH.

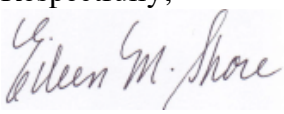
Financial Report (2015):
Funds available: $17,456.55 (2015 funds; 15,000 euro, received January 2015)

	Received	Spent	Balance
POH Researchers		$16,016	
Overhead		$1,441	
Total	$17,457	$17,457	$0

In 2015, funding from the Italian POHA was used for partial support for a Research Specialist to conduct DNA sequence analysis (Project #1 above) and to contribute to support of studies by postdoctoral researchers on the effects of *GNAS* mutations on cell fate decisions and skeletal bone quality. The results of some of our studies have been presented at scientific conferences in 2015 and are in preparation for manuscript publication in 2016.

Funding through the Italian POHA has been important in continuing to reach a better understanding of POH that will lead to therapeutic options. The support of the IPOHA is greatly appreciated.

Respectfully,



Eileen M. Shore, PhD
Professor of Orthopaedic Surgery and Genetics
Perelman School of Medicine at the University of Pennsylvania
email: shore@mail.med.upenn.edu