Perelman School of Medicine
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Report to Dr. Roberto Bufo and the Italian POHA – December 2016

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. In a key discovery by our research group, heterozygous inactivating mutations in the *GNAS* gene were identified as the cause of POH. *GNAS* has many critical roles in our cells, but heterotopic ossification in POH is a very specific consequence. Identifying the specific downstream effects of *GNAS* inactivation that lead to ectopic bone formation will identify specific treatment targets for POH.

In 2016, studies supported in part by the Italian POHA are:
1. Evaluate 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. Investigate 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 the skeleton and in heterotopic ossification, in order to identify therapeutic targets.
3. Develop and test an improved *in vivo* mouse model for POH heterotopic ossification that will be used to further understand ectopic bone formation in POH and for future pre-clinical drug testing.

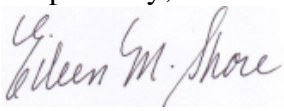
Financial Report (2016):
Funds available: $19,261 (2016 funds; 18,000 euro, received March 2016)

	Received	Spent	Balance
POH Researchers		$17,671	
Overhead		$1,590	
Total	$19,261	$19,261	$0

In 2016, funding from the Italian POHA was used for partial support of postdoctoral researchers examining the effects of *GNAS* mutations on cell fate decisions and our important progress on developing and testing our POH mouse model. The results of some of our studies have been presented at scientific conferences in 2016 and a manuscript describing some of our work is under review for publication.

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

Respectfully,



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