Perelman School of Medicine
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Report to Dr. Roberto Bufo and the Italian POHA – November 2020

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 (POHA) and the Italian POHA (IPOHA). 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. Research to investigate the molecular and cellular targets of *GNAS* inactivation that lead to ectopic bone formation in order to identify specific treatment targets for POH is continuing.

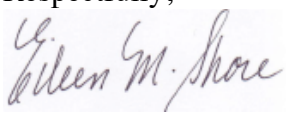
Studies supported in part by the Italian POHA are:
1. Evaluate the DNA sequence of the *GNAS* gene in patients who have received a clinical diagnosis of POH. These studies investigate the correlation between clinical presentation and specific gene mutations as well as increase our understanding of the range of mutations that cause POH.
2. Using a recently developed mouse model, investigate POH heterotopic ossification *in vivo*. These studies are revealing the earliest effects of *GNAS* mutation that lead to ectopic bone formation in POH, including changes to tissues prior to formation of heterotopic ossification. We are in the process of submitting a manuscript that will report some of our data. A graduate student, who has previously been mainly supported through a NIH research fellowship, continues to work on this and other POH projects.
3. During 2020, we have begun to develop strategies to use the POH mouse model in pre-clinical testing for POH.

Financial Report (2020):
Funds available: $19,015 (2020 funds; 18,000 euro, received January 2020)

	Received	Spent	Balance
POH Researchers		$9,493	
Lab experiment support		$9,522	
Total	$19,015	$19,015	$0

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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