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Report to Dr. Roberto Bufo and the Italian POHA – November 2018

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 molecular and cellular effects of *GNAS* inactivation that lead to ectopic bone formation will identify specific treatment targets for POH.

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. To understand the cellular origins and molecular pathways in bone formation that are controlled by *GNAS* gene products, 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. Use a recently developed mouse model for *in vivo* investigations of POH heterotopic ossification to further understand the earliest effects of *GNAS* mutation that lead to ectopic bone formation in POH. This model will also be important for future pre-clinical drug testing.

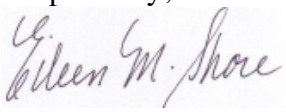
In 2018, we have made substantial progress using our POH mouse model as a system to better understand how *GNAS* mutation changes tissues prior to formation of heterotopic ossification. The results of some of our studies have been presented and recognized by awards at scientific conferences in 2018.

Financial Report (2018):
Funds available: $18,114 (2018 funds; 15,000 euro, received February 2018)

	Received	Spent	Balance
POH Researchers		$7,526	
Lab experiment support		$10,588	
Total	$18,114	$18,114	$0

We are pleased to report that a graduate student working on POH projects was awarded a research fellowship by the NIH this year. This has provided additional funds to support lab experiments. 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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