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**Report to Dr. Roberto Bufo and the Italian POHA – December 2017**

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 2017, 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. 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.

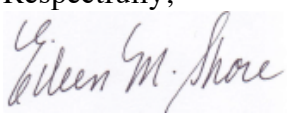
**Financial Report (2017):**
Funds available: $16,725 (2017 funds; 16,000 euro, received February 2017)

| | Received | Spent | Balance |
|---|---|---|---|
| POH Researchers | | $15,344 | |
| Overhead | | $1,381 | |
| Total | $16,725 | $16,725 | $0 |

In 2017, funding from the Italian POHA was used for partial support of researchers examining the effects of *GNAS* mutations on cell fate decisions and to continue our progress in characterizing and using our POH mouse model. The results of some of our studies have been presented at scientific conferences in 2017 and a manuscript describing the effect of *GNAS* inactivation on skeletal bone was published.

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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