Perelman School of Medicine
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Report to Dr. Roberto Bufo and the Italian POHA – August 2012

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 recently published manuscripts describing the effects of GNAS mutation on adipose-derived progenitor cells (Pignolo et al., 2011; Liu et al., 2012). We have also initiated investigations to develop RNAi strategies of individual GNAS products in order to further understand the specific regulators for GNAS-directed osteogenesis.

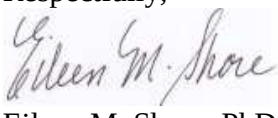
Financial Report (January-July 2012):
Funds available:
$25,325 (2012 funds) + $1,045 (June 2011 carry forward) + $11,848 (Dec 2011 carry forward)= $38,218

	Received	Spent to Date	Balance
POH Researchers		35,062	
Overhead		3,156	
Total	$38,218	$38,218	$0

In 2012, 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 postdoctoral researchers (Jan-Jan Liu, PhD and Josef Kaplan, PhD) for studies on the effects of *GNAS* mutations on cell fate decisions (Project #2 above).

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,



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