

**SIXTH INTERNATIONAL ALKALINE PHOSPHATASE and
HYPOPHOSPHATASIA SYMPOSIUM
“From Bench to Bedside”
Huningue, Alsace, France
May 16-19, 2012**

Welcome, Bienvenue, Willkommen!

Dear Participants:

Welcome to Huningue, Alsace, France, for four days of intense scientific and personal interactions while enjoying the hospitality of the dedicated volunteers of “Hypophosphatasia Europe”, a public not-for-profit organization that aims to gather and disseminate information on APs to help patients with HPP and their families.

This will be the second time that basic researchers, physicians and advocacy group members gather in Huningue to discuss the latest information pertaining to the function of APs and therapies being developed for the management of AP-associated disorders.

The previous symposium in 2007 witnessed the announcement of the first successful pre-clinical trials of enzyme replacement therapy for HPP in mice. Since then, clinical trials of life-threatening HPP have been completed with remarkable results and phase II/III clinical trials on HPP patients with adult disease have been initiated.

This Symposium will highlight the wealth of clinical data that has been obtained on the management of HPP patients, while also discussing new information about other pathophysiological conditions related to alterations in AP structure and function.

We wish to thank the volunteers of Hypophosphatasie Europe for their dedication and help with all the logistical arrangements that have made this scientific meeting possible. We also wish to thank our financial sponsors, listed on the next page, for providing us the funds needed to organize this conference. Finally, we wish to thank you, the participants, for submitting significant new data for presentation and for sharing your expertise, knowledge and questions with the audience. It is the hope of the organizing committee that you will participate actively in the sessions and enjoy your visit to Huningue. Please let us know if there is anything we can do to make your stay more pleasant

José Luis Millán, Steve Ursprung, Agnès Bloch-Zupan and Etienne Mornet
Co-organizers.

The 6th International Alkaline Phosphatase and Hypophosphatasia Symposium was supported by:

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Program

Wednesday, May 16

13:00-14:00 Registration

14:00 Welcome and Opening of the meeting

14:15-15:15

Keynote lecture: **Michael P. Whyte** (St Louis, MO, USA) “Pathogenesis and treatment of hypophosphatasia”

15:15-15:40 Pause

15:40-17:40

SESSION 1: Pathophysiology of biomineralization

15:40-16:20

Keynote communication: **José Luis Millán** (La Jolla, CA, USA) “Mechanisms of initiation of skeletal mineralization”

16:20-16:40

Pietro Ciancaglini (Ribeirao Preto, Brazil): Nanotechnology in biomineralization: proteoliposomes as MVs biomimetics

16:40-17:00

Ana Maria S. Simão (Ribeirao Preto, Brazil): PiT-1 reconstitution into liposomes for biomineralization studies.

17:00-17:20

Santiago Gomez (Cadiz, Spain): Alkaline phosphatase in bone: insight from zinc mapping studies

17:20-17:40

Campbell Sheen (La Jolla, CA, USA) TNAP upregulation in vascular smooth muscle cells is sufficient to cause medial vascular calcification

17:45 Welcome reception

20:00 Dinner

Thursday, May 17

09:00-12:40

SESSION 2: Diagnosis of HPP

09:00-09:40

Keynote communication: **Andrea Superti-Furga** (Switzerland)

09:40-10:00

Agnès Bloch-Zupan (Strasbourg, France): Oro-dental features in hypophosphatasia: a valuable phenotype for disease diagnosis and evaluation of future treatment outcomes

10:00-10:20

Michael P. Whyte (St-Louis, MO, USA): “Atypical femoral fractures” during biphosphonate exposure in adult hypophosphatasia

10:20-10:40

Michael P. Whyte (S- Louis, MO, USA): Fracture burden in adults with hypophosphatasia

10:40-11:00

Katherine L Madson (St Louis, MO, USA): Hypophosphatasia: A series of diagnosis missteps

11:00-11:30 Coffee break

11:30-11:50

Maurice Audran (Angers, France): Bone quality changes in 3 cases of hypophosphatasia: a FTIRI study

11:50-12:10

Michael P. Whyte (St-Louis, MO, USA): Acute severe hypercalcemia after traumatic fracture and immobilization in an adult with Hypophosphatasia complicated by renal failure

12:10-12:30

Mark A. Nunes (San Diego, USA): Identifying individuals at risk for hypophosphatasia using

an electronic medical record (EMR)

12:30-14:00 Buffet lunch

14:00-16:00

Session 2 (continued): Diagnosis of HPP

14:00-14:20

Keichi Ozono (Osaka, Japan): Two common mutations in the ALPL gene in Japanese patients with Hypophosphatasia

14:20-14:40

Hideo Orimo (Tokyo, Japan): Characterization of a deletion in tissue-nonspecific alkaline phosphatase (p.F327del) as the third frequent mutation in the Japanese patients with hypophosphatasia

14:40-15:00

Takeshi Taketani (Shimane, Japan): Clinico-genetical characteristics of Japanese patients with Hypophosphatasia

15:00-15:20

Atsushi Watanabe (Tokyo, Japan): Perinatal (lethal) type of hypophosphatasia resulting from paternal isodisomy of chromosome 1

15:20-15:40

Barbara Gasse (Paris, France): Evolutionary analysis of ALPL validates and predicts human mutations leading to hypophosphatasia

15:40-16:00

Etienne Mornet (Versailles, France): In silico scoring of ALPL gene mutations help to distinguish severe and moderate phenotypes in hypophosphatasia

17:00 Sailing on the Rhine and dinner

Friday, May 18

09:30-11:10

SESSION 3: Multi-systemic aspects of hypophosphatasia

09:30-10:10

Keynote communication: **Mark J Zylka** (Chapel Hill, USA) "Role of TNAP and other ectonucleotidases in pain mechanisms"

10:10-10:30

Caroline Fonta (Toulouse, France): Bone TNAP

in the brain: functions in neurotransmissions

10:30-10:50

Per Magnusson (Linköping, Sweden): Alkaline phosphatase bone isoforms in skeletal mineralization and vascular calcification

10:50-11:10

Susana Guerreiro (Porto, Portugal): Crosstalk between fibroblasts and endothelial cells promotes angiogenesis in vitro: putative role of alkaline phosphatase, growth factors and collagen

11:10-11:40 Coffee break

11:40-13:20

SESSION 4: AP-related diseases and animal models

11:40-12:20

Keynote communication: **Daniel Vaiman** (Paris, France) "Pregnancy failure and alkaline phosphatases: from mouse genetics to human disease"

12:20-12:40

Miles Thompson (Toronto, Canada): Phenotypic variability in Mabry Syndrome: evidence for genetic heterogeneity

12:40-13:00

Cecilia H. Linder (Linköping, Sweden): Characterization of alkaline phosphatase in mice

13:00-13:20

Birgit Mentrup (Wuerzburg, Germany): In vitro characterization of TNSALP mutations from two novel mouse models for hypophosphatasia

13:20-14:30 Buffet lunch

14:30-18:00

SESSION 5: Treatments of hypophosphatasia

14:30-15:10

Keynote communication: **Takashi Shimada** (Tokyo, Japan) "Gene therapy for lethal murine hypophosphatasia"

15:10-15:30

Michael P. Whyte (St Louis, MO, USA): Hypophosphatasia - enzyme replacement therapy (asfotase alfa) decreases TNSALP sub-

trate accumulation and improves functional outcomes in affected adolescents and adults

15:30-15:50

Christine Hofmann (Wuerzburg, Germany): Enzyme replacement therapy in different clinical phenotypes of hypophosphatasia – a presentation of two cases

15:50-16:10

José Luis Millán (La Jolla, USA): Enzyme replacement prevents enamel defects in hypophosphatasia mice

16:10-16:40 Pause

16:40-17:00

Osamu Iijima (Tokyo, Japan) Ex vivo gene therapy of severe infantile hypophosphatasia model mice using lentiviral transduced bone marrow cells

17:00-17:20

Hanako Sugano (Tokyo, Japan): Successful gene therapy in utero for lethal murine hypophosphatasia

17:20-17:40

Jean-Pierre Salles (Toulouse, France): Growth hormone increases growth velocity and alkaline phosphatase level in children with hypophosphatasia

17:40-18:00

Jean-Pierre Salles (Toulouse, France): Bisphosphonates in hypophosphatasia: not the evil?

18:00 Aperitif and dinner

Saturday, May 19

9:00-12:00

SESSION 6: Managing the upcoming treatments - Panel discussion Q&A session for lay audience

9:00-09:40

Keynote communication: **Franz Jakob** (Wuerzburg, Germany): “Hypophosphatasia: upcoming treatments”

9:45-12:00

Q&A with panel of HPP experts