

Pre-Symposium: Lesch-Nyhan Disease Research Foundation

Chairs: Friedmann, T.; Jinnah, H.A..

Plenary Session: Sunday June 24 1:00 - 4:10 pm

1:10-1:30 (I1) Nyhan, W.N. Lesch-Nyhan Disease

1:40-2:00 (I2) O'Neill, P. Mutation Carrier Testing in Lesch-Nyhan Disease Families: HPRT1 Mutant Frequency and Mutation Analysis with Peripheral Blood T Lymphocytes

2:10-2:30 (I3) Friedmann, T. Gene Expression Profiles in HPRT-deficient Mouse Brain

3:10-3:30 (I4) Jinnah, H.A. New Trends in the Neurobiology of Lesch-Nyhan Disease

3:40-3:55 (O1) Shirley, T. HPRT-deficient human neuroblastomas as a model for Lesch-Nyhan Disease

3:55-4:10 (O2) Visser, J. Treatment of Lesch-Nyhan Disease with Levodopa: an open-label trial

Poster Session: Sunday June 24 (authors present 4:10 - 5:00 pm)

P1 Yamada, Y. Molecular analysis of hypoxanthine guanine phosphoribosyltransferase (HPRT) deficiencies: Novel mutations and the spectrum of Japanese mutations

P2 Cerboni, B. NAD glycohydrolase activity in Lesch-Nyhan erythrocytes
(**WITHDRAWN**)

P3 Verdu, A. Urinary guanidinoacetate and creatine levels in patients with HPRT deficiency

P4 Bertelli, M. Study of mRNA editing level in serotonin receptor 2C (HTR2C) from HPRT Knock-Out mouse brain (mouse model for Lesch-Nyhan Disease)

(**WITHDRAWN**)

PP07 Symposium

Session 1: Mechanistic Advances in Gout and Hyperuricemia

Chairs: Becker, M.; Kamatani, N.

Plenary Session: Monday June 25 8 :00 - 10 :00 am

8:00-8:30 (I5) Endou, H. Current knowledge of renal urate transport

8:40-8:55 (O3) Taniguchi, A. Association of SNPs in SLC22A12 gene with the development of gout in Japanese

8:55-9:10 (O4) Becker, M.A. Determinants of the clinical outcomes of gout during the first year of urate-lowering therapy

9:10-9:25 (O5) Hershfield, M.S. Contribution of tophaceous urate deposits to the exchangeable urate pool: revisiting an old question with new methods during treatment of gout with pegylated mammalian uricase (PEG-Uricase)

9:25-9:55 (I6) Kamatani, N. Mutations in uromodulin gene identified as the cause of underexcretion-type gout and hyperuricemia associated with chronic renal insufficiency through linkage analysis

Session 2: Hyperuricemia, Metabolic and Cardiovascular Disease: Associations and Mechanisms

Chairs: Johnson, R.; Puig, J.G.

Plenary Session: Monday June 25 10:30 am – 12:30 pm

10:30-11:00 (I7) Johnson, R. How could an antioxidant such as uric acid cause cardiovascular disease?

11:10-11:30 (I8) Puig, J.G. Hyperuricemia in patients with the metabolic syndrome: epidemiology, pathophysiology and clinical significance

11:40-11:55 (O6) Cormaci, G. AMP- and adenosine-deaminase up-regulation contribute to enhanced oxidative stress in murine heart failure

11:55-12:10 (O7) Leoncini, R. Antioxidant status and purine bases in carotid artery plaque

12:10-12:25 (O8) Yuen, A. new assay for determination of AMP-activated protein kinase using Liquid chromatography with Electrospray/ion trap tandem Mass spectrometry

Session 3: Inborn Errors of metabolism: Strategies and Analytical Methods

Chairs: Smolenski, T.; Snyder, F.

Plenary Session: Monday June 25, 1:30 – 3:30 pm

1:30-2:00 (I9) Christopherson, R. Fludarabine induces differential expression of proteins in human leukemia and lymphoma cells

2:10-2:25 (O9) Snyder, F. Application of metabolomic principles to the analysis of disorders of nucleotide metabolism reveals previously unrecognized metabolic perturbations

2:25-2:40 (O10) Sebesta, I. Unusual manifestation of Kelley-Seegmiller syndrome

2:40-2:55 (O11) Stiburkova, B. Analysis of hypouricemic patients with respect to the SLC22A12 (URAT1) gene

2:55-3:25 (I10) Smolenski, R.T. Application of mass spectrometry for measurements of metabolite levels, enzyme activities and in vivo metabolic fluxes

Session 4: Purines/Pyrimidines in Brain

Chairs: Jinnah, H.A.; Rathbone, M.

Plenary Session: Monday June 25, 4:00 – 6:00 pm

4:00-4:30 (I11) Rathbone, M.P. The neurotrophic roles of extracellular non-adenine-based purines

4:40-4:55 (O12) Jiang, S. Remyelination after chronic spinal cord injury is associated with proliferation of endogenous adult progenitor cells after systemic administration of guanosine

5:00-5:30 (I12) Jinnah, H.A. Uric acid & the brain: friend, foe, or folly?

5:40-5:55 (O13) Torres, R.J. The diagnosis of HPRT deficiency in the 21st century

Session 5: Purines/Pyrimidines and Cancer

Chairs: Mitchell, B.; Peters, G.

Plenary Session: Tuesday June 26, 8:00 – 10:30 am

8:00-8:25 (I13) Peters, G. The role of thymidine phosphorylase/platelet-derived endothelial cell growth factor (TP/PDECGF) in cancer as an antiangiogenic target and modulator of anticancer activity

8:30-8:45 (O14) Van Kuilenburg, A. Clinical pharmacokinetics of 5-fluorouracil in patients heterozygous for the IVS14+1G>A mutation in the dihydropyrimidine dehydrogenase gene

8:45-9:00 (O15) Bjinsdorp, I. Trifluorothymidine induces cell death by both caspase activation and caspase independently

9:00-9:15 (O16) Mitchell, B. Guanine nucleotide depletion mediates translocation of nucleolar proteins, including RNA helicase A (DHX-9)

9:15-9:30 (O17) Fyrberg, A. RNAi silencing of deoxycytidine kinase and deoxyguanosine kinase as a tool to study nucleoside analogue activity and resistance mechanisms in human leukemic CEM cells

9:30-9:45 (O18) Molina-Arcas, M. Transcriptomic response of the nucleoside-derived drug 5DFUR in breast cancer MCF7 cells. Role of equilibrative nucleoside transporter-1 (hENT1) and aquaporin-3 (AQP3)

9:45-10:00 (O19) McLennan, A. Correlation of the intracellular purine nucleotide Ap3A with induced apoptosis in Fhit-positive cells

10:00-10:25 (I14) Carson, D. Regulation of inflammation by nucleotides reactive with toll-like receptors

Session 6: Extracellular Metabolism and Receptors

Chairs: Blackburn, M.; Cronstein, B.; Thompson, L.

Plenary Session: Tuesday June 26, 11:00 am – 1:00 pm

11:00-11:30 (I15) Robson, S.C. The ectonucleotidase CD39/NTPDase1 is a key integrator of vascular inflammation and immunity

11:40-11:55 (O20) Faria, M. Decreased purinoceptor-mediated tonus of human corpus cavernosum from men with vasculogenic erectile dysfunction

11:55-12:10 (O21) Thompson, L. Regulation of leukocyte migration across endothelial barriers by ecto-5-nucleotidase-generated adenosine

12:10-12:25 (O22) Gorodeski, G. Hyper-methylation of the 5UTR-Exon-1 region of the human P2X7 gene downregulates expression of P2X7 mRNA in cancer epithelial cells and abrogates P2X7-mediated apoptosis

12:25-12:55 (I16) Cronstein, B. Purine growth factor 1; adenosine and its receptors

Session 7: Purine/Pyrimidine Transport

Chairs: Cass, C.; Graves, L.

Plenary session: Wednesday June 27, 8:00 – 10:00 am

8:00-8:30 (I17) Cass, C. Molecular and pharmacological studies of the role of human nucleoside transporters in chemotherapy with anticancer nucleoside drugs

8:40-8:55 (O23) Leisewitz, A.V. Regulation of ENT1 expression and ENT1-Dependent Nucleoside Transport by Src and cJun N-terminal kinases

8:55-9:10 (O24) Giovannetti, E. Expression of the nucleoside transporters hENT1 and hCNT1 in pediatric acute myeloid leukemia

9:10-9:25 (O25) Ichida, K. Ancestral origin of the G774A mutation in SLC22A12 causing renal hypouricemia in Japan

9:25-9:55 (I18) Pastor-Anglada, M. Physiological roles of nucleoside T transporter proteins: from absorption to cell signaling

Session 8: Purine/Pyrimidine Metabolism in Protozoans, Viruses, and Other Non-Mammalian Species

Chairs: Balzarini, J.; Schramm, V.

Plenary Session: Wednesday June 27, 10:30 am – 12:30 pm

10:30-11:00 (I19) Ullman, B. Genetic analysis of purine metabolism in *Leishmania donovani*

11:10-11:25 (O26) Switzer, R.L. Cross-regulation of pyrimidine biosynthesis by purine activation: A general phenomenon in Gram-positive bacteria

11:25-11:40 (O27) Bjornberg, O. A novel pathway for degradation of nucleic acid precursors

11:40-11:55 (O28) Schnackerz, K.D. Degradation of pyrimidines: malonate semialdehyde, the transamination product of β -alanine

11:55-12:25 (I20) Balzarini, J. Acyclic nucleoside phosphonates: a unique class of stable nucleotide analogues with a variety of antiviral and anticancer applications and differential metabolic activations

Session 9: Molecular Mechanisms of Disease

Chairs: Eriksson, S.; Hershfield, M.

Plenary Session: Wednesday June 27, 3:45 – 5:45 pm

3:45-4:15 (I21) Eriksson, S. Molecular mechanisms of mitochondrial DNA depletion diseases caused by deficiencies in enzymes in purine and pyrimidine metabolism

4:25-4:40 (O29) Van Kuilenburg, A. Identification of two novel mutations in the dihydropyrimidine dehydrogenase gene in a patient presenting with hematuria

4:40-4:55 (O30) Morisaki, T. Minimal Change Nephropathy in AMPD2-Deficient Mice

4:55-5:10 (O31) Whitehead, J. Investigating a potential role for inosine-5 monophosphate dehydrogenase (IMPDH) in adipogenesis

5:10-5:25 (O32) Block, E. Interferon-gamma (IFN γ) blocks adenosine receptor-mediated induction of collagen production in hepatic stellate cells

5:25-5:40 (O33) Snyder, F. Gene expression array analysis reveals early cellular changes in the PNP deficient mouse thymus

5:40-5:55 (O34) Joachims, M. Correction of adenosine deaminase deficient human thymocyte development in vitro by inhibition of deoxynucleoside kinases

Session 10: Recent Advances in Purine/Pyrimidine Enzyme Regulation

Chairs: Bontemps, F.; Sabina, R.L.

Plenary Session: Thursday June 28, 8:00 – 10:00 am

8:00-8:30 (I22) Hedstrom, L. IMP dehydrogenase-linked retinitis pigmentosa

8:40-8:55 (O35) Sabina, R.L. Accelerated adenine nucleotide catabolism and calmodulin activation of erythrocyte AMP deaminase (AMPD3): a paradigm for clinical disorders of disturbed erythrocyte calcium homeostasis?

8:55-9:10 (O36) Leoncini, R. Some aspects of the adenosine kinase reaction

9:10-9:25 (O37) Higgins, M. Regulation of Human CTPS1 by GSK-3 Beta Phosphorylation

9:25-9:55 (I23) Bontemps, F. Post-translational regulation of deoxycytidine kinase activity: a key role for phosphorylation of Ser-74

Session 11: Protein Structure and Catalytic Mechanism

Chairs: Smith, J.; Switzer, R.

Plenary Session: Thursday June 28, 10:30 am – 12:30 pm

10:30-11:00 (I24) Smith, J. To be announced

11:10-11:25 (O38) Wallden, K. Structure of human cytosolic 5-nucleotidase II: Insights into regulation and substrate recognition

11:25-11:40 (O39) Nishino, T. Molecular mechanism of transition from xanthine dehydrogenase to xanthine oxidase

11:40-11:55 (O40) Urusova, D. SAICAR synthase: L-aspartate binding site mobility is a requirement for catalytic activity

11:55-12:25 (I25) Ealick, S. E. Catalytic strategies for the cyclization reactions in purine biosynthesis

Poster Session I: Monday June 25/Tuesday June 26 (authors at posters 2:35-3:50 pm on Tuesday, June 26)

NOTE: This session also includes posters P1-P4 from the LNDRF Pre-Symposium

Mechanistic Advances in Gout and Hyperuricemia

P5 Puig, J.G. Asymptomatic hyperuricemia: impact of ultrasonography

P6 Inokuchi, T. Effects of allopurinol on beer-induced increases in plasma concentrations of purine bases and uridine

P7 Montoya, F. An unusual patient with hypothyroidism, tophaceous gout and marked joint destructions

P8 Moriwaki, Y. Effect of acarbose on the increased plasma concentration of uric acid induced by sucrose ingestion

Hyperuricemia, Metabolic and Cardiovascular Disease: Associations and Mechanisms

P9 Puig, J.G. Serum urate, metabolic syndrome and cardiovascular risk factors. A population-based study

P10 Yamamoto, T. Effects of sucrose ingestion on purine bases and uridine

P11 Chen, S-Y. Metabolic syndrome associated with male gout in different age strata

P12 Tsutsumi, Z. High prevalence of metabolic syndrome in Japanese patients with gout

Inborn Errors of metabolism: Strategies and Analytical Methods

P13 Torres, R.J. Complete and Partial HPRT deficiency with reduced enzyme expression and normal coding region

P14 Vyskocilova, P. Activity of ITPase in dry blood spots by capillary electrophoresis

P15 Vyskocilova, P. Membrane transport and metabolism of aminoimidazole ribosides in erythrocytes

P16 Vyskocilova, P. Activity of thiopurine methyltransferase by capillary electrophoresis

P17 Slanar, O. Fatal myelotoxicity after azathioprine treatment.

Purines/Pyrimidines and Cancer

P18 Giovannetti, E. Correlation between cytidine deaminase genotype and gemcitabine deamination in blood samples

P19 Bastin-Coyette, L. Mechanisms of 2-chloroadenosine cytotoxicity in B-leukemic cells

P20 Skoglund, K. Explaining TPMT genotype/phenotype discrepancy by identification of a novel sequence variant, TPMT*23

P21 Van Kuilenburg, A. Increased dihydropyrimidine dehydrogenase activity associated with mild toxicity in patients treated with 5-fluorouracil containing chemotherapy

P22 Inai, K. Association between Ecto-5-nucleotidase and Vimentin in Aggressive Breast Cancer Cells

P23 Codacci-Pisanelli, G. Selective protection by uridine of the RNA mediated growth inhibition by 5-fluorouracil (FU), but not the thymidylate synthase mediated growth inhibition by FU-leucovorin

P24 Giovannetti, E. Functional inactivity and mutations of p53 affect differently the sensitivity to 5-fluorouracil and antifolate inhibitors of thymidylate synthase (TS) by altering TS levels in colorectal cancer cells

P25 Bjerke, M. Reduced levels of mitochondrial DNA increases the toxicity of araG

P26 Leoncini, R. Gene expression of purine metabolism in human colorectal cancer

P27 Eriksson, S. Silencing of 5-nucleotidases enhance nucleoside analogues cytotoxicity in leukemic cells

P28 Tsutani, H. Application of monosodium urate crystal as a carrier for idiotype tumor vaccine

Poster Session II Wednesday June 27/Thursday June 28. (Authors at posters 2:15-3:30 pm on Wednesday, June 27)

Extracellular Metabolism and Receptors

P29 Che, J. Adenosine A2A receptor occupancy stimulates collagen expression by hepatic stellate cells via pathways involving PKA, SRC and ERK 1/2 signalling cascade or P38 MAPK signalling pathway

P30 Lui, H. Adenosine A2A receptor occupancy regulates expression of multiple genes involved in wound healing

P31 Smolenski, R.T. Attenuation of the mechanisms of rejection in xenotransplantation by expressing human ecto-5-nucleotidase in pig endothelial cells

Molecular Mechanisms of Disease

P32 Peng, Z. Ecto-5-nucleotidase (CD73)-mediated adenosine production promotes the fibrosis formation in a model of CCL4-induced liver fibrosis

P33 Van Kuilenburg, A. Clinical variability in two siblings with a dihydropyrimidinase deficiency

P34 Jurecka, A. Adenylosuccinate lyase deficiency: Clinical, biochemical and molecular findings in 7 Polish patients

P35 Slominska, E. Metabolism of 4-pyridone-3-carboxamide-1--D-ribonucleoside triphosphate and its nucleoside precursor in the erythrocytes, endothelium and cardiomyocytes

P36 Taniguchi, A. Genotype-phenotype correlation in Japanese patients with APRT deficiency

P37 Slanar, O. Polymorphisms of the TPMT gene in the Czech healthy population and patients with inflammatory bowel disease

Recent Advances in Purine/Pyrimidine Enzyme Regulation

P38 Smal, C. Deoxycytidine kinase activity is positively regulated by phosphorylation of Ser-74 in B-cell chronic lymphocytic leukemia lymphocytes

P39 Smal, C. Deoxycytidine kinase is phosphorylated in vitro by Casein kinase I delta

P40 Wang, L. 5-Bromovinyl 2-deoxyuridine (BvdU) phosphorylation by human thymidine kinase 2 and 1 and its use in selective measurement of TK2 activity in crude extracts

P41 Slominska, E. Cytoprotective effects of nicotinamide derivatives in endothelial cells

P42 Borkowski, T. Pharmacological inhibition of AMP-deaminase in rat cardiac myocytes

P43 Borkowski, T. Modulation of AMP deaminase in rat hearts subjected to ischemia and reperfusion by purine riboside

Protein Structure and Catalytic Mechanism

P44 Okamoto, K. Potent inhibitors of xanthine oxidoreductase : Mechanisms of inhibition and crystal structures of the enzyme-inhibitor complexes

P45 Matsumura, T. Mutational analysis of human xanthine oxidase: Roles of the amino acid residues around the active site in purine oxidation reaction

P46 Lovelace, L.L. Structure of human thymidylate synthase (hTS) with stabilized active conformation of loop 181197

P47 Canyuk, B. The role for glutamic acid at the position 196 in human hypoxanthine phosphoribosyltransferase (HPRT) is investigated using site-directed mutagenesis and functional analysis

Miscellaneous

P48 Leoncini, R. The testosterone regulation of rat liver on purine metabolism

P49 Kaneko, K. Contents of purine bases in soybean-derived food and in some Japanese vegetables and mushrooms

P50 Vyskocilova, P. Normal reference values of nucleotides in cultured skin fetal fibroblasts

P51 Hosoyamada, M. Production and characterization of transgenic mice harboring mutant human UMOD gene