



International Society for Enzymology (ISE)

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INTERNATIONAL CONFERENCE ON LABORATORY MEDICINE

ENZYMES: OLD MOLECULES WITH NEW CLINICAL APPLICATIONS

Padua, Italy, October 24 – 26, 2006

At 6.30 pm on the evening of Monday October 24th, a band of individuals proudly wearing the registration insignia of the above International Conference was discreetly admitted to the Scrovegni Chapel in Padua, where for 30 minutes they were permitted to examine the celebrated frescoes painted by the great Giotto on a commission from a moneylender, who thereby hoped to redeem his soul and those of his family from the flames of hell. Ejected before the carbon dioxide they were communally exhaling could do further damage to the delicate paintings counted among the greatest treasures of early Renaissance art, they walked the short distance to the Museo Ermitani where they were expertly guided through a special exhibition devoted to Andrea Mantegna, a son of Padua who had died 500 years ago. His legacy of painting is inscribed on the walls of historic buildings in Mantua and Verona. Alas, those that he left in his native city were reduced to little pieces of coloured plaster that local experts are painstakingly seeking to reconstitute, following devastating bomb-damage towards the end of World War II. Fortunately, many of his smaller but no less great works survive in galleries throughout the world, and several had, like us, made the long journey to Padua to form part of this retrospective tribute to the painter and his associates. Minds and souls duly nourished, the company adjourned to the Egyptology Section of the Museum where the exigencies of the stomach now received attention. Under the scrutiny of dignitaries dead for 5,000 years and now confined to their intricately decorated vertical coffins, the assembled company was wined and dined in a manner befitting the royalty whose ancient remains bore witness to the event, and with a gastronomic skill that would have won a star or two from aficionados of the Michelin Red Guide.

What has all of this to do with Science? Anywhere else, the answer would be *nothing at all*, but here in Italy, Science, History and Culture form a seamless continuum, and one moves effortlessly between the three elements. **Jack Ladenson, St Louis, MO, USA**, clearly grasped this connection during the opening lecture of the First Session: *Enzymes in Cardiovascular Diseases* that took place on the afternoon of October 24 at the Aula Magna del Bo in the ancient and original University complex. His talk was true to its title, *Historical Background*, and made numerous references to many of the giants, such as Arthur Karmen,

Gabor Szasz and Sidney Rosalki, whose contributions nearly 50 years ago had led, first, to the establishment of the subject and ultimately to that of this Society. Moving on to his own seminal work on the use of monoclonal antibodies to CK-subunits to establish radio-immunoassays for their measurement, he ended with a hymn in praise of cardiac-Troponin I, cTnI, that he regarded as the most clinically valuable current cardiac marker.

Having arrived by air only a few hours earlier, **Allan Jaffe, Rochester, MI, USA**, lost no time in going beyond this protein that we have known for two decades in his presentation, *Cardiac Markers: State-of-the-Art*. He spoke enthusiastically about the potential merits of two relatively new players on the block, B-type natriuretic peptide and Lipoprotein-related phospholipase A2, but still could not avoid the claims of history. It was gratifying to hear him describe work published shortly before his untimely death by Angelo Burlina, the *de facto* founder of ISE to whose memory the entire Meeting was dedicated; and in describing C-reactive protein, CRP, as a very important prognostic factor when measured a few days after infarction, he was paying tribute to a molecule that was identified shortly after I graduated from Medical School, although its role as a cardiac marker was not then known.

After the Americans, it was the turn of the Italians to take the floor. Citing St Paul's Letter to the Corinthians (being in Italian, although the original was probably in Hebrew, I am ashamed to say that I cannot reproduce the exact quotation), **Martina Zaninotto, Padua**, described *New Biochemical Markers: From Bench to Bedside*. This was an exciting presentation that, despite the language barrier, was easy to follow because of the excellence of her Anglo-Saxon slides. Focusing upon inflammatory cytokine release and markers of specific complications of atherosclerosis such as plaque destabilization and rupture, as well as cardiac ischaemia and necrosis *per se*, she described the roles of Myoglobin, Heart-type fatty acid-binding protein, and Glycogen phosphorylase-BB. In reference to its possible pathogenetic role, she spoke of CRP as both a "maker" and a "marker" of disease, while, drawing an analogy from the game of chess, the superiority of High-sensitivity CRP was likened to the "Pawn being promoted to the Queen".

In her lecture *Polymorphisms and Gene Expression of Enzymes Involved in Cardiovascular Diseases*, **Giuliana Fortunata, Naples**, began with an account of genetic risk factors for coronary heart disease. Among these, the 5-Lipoxygenase-activating protein, Metalloproteinases and Paraoxanases (PON)-1 and -2 were of special interest. The latter enzymes are highly polymorphic; mice deficient in PON-2 are especially susceptible to developing atherosclerosis on a high fat diet, while in humans, lower levels are associated with a higher severity of arterial plaques.

It was the task of a former President of IFCC, looking more youthful than is usual in a man of his ripe years, **Gerard Siest, Nancy, France** to conclude this Symposium with an account of *The Pharmacogenomics and Pharmacoproteomics of Cardiovascular Drugs*. Listing 18 different drug classes, and pointing out that many of the genes concerned in their metabolism are subject to more than 100 genetic variants, he raised the prospect of detaining the audience until midnight or beyond. Sensibly, however, he restricted his content to antihypertensive drugs and their interaction with microsomal cytochromes, especially Cyp 2D6 and Cyp 2C. His final plea for personalized antihypertensive drug therapy based on knowledge of the individual's drug-related enzyme polymorphisms was delivered in time for a mass exodus shortly before the scheduled conclusion at 6.30 pm.

After a buffet dinner at the Caffè Pedrocchi, an establishment noted for more than 150 years as the city's focal gathering-point for poets, politicians and other trouble-makers, the Evening Program continued with a concert at the Baptistery of the Cathedral. Begun in 1075 and covered from floor to ceiling by an astonishing cycle of paintings completed in 1378 by Menabuoi, it provided an exquisite setting for a series of works by Bach and Mozart performed by the gifted soprano Roberta Canzian, accompanied by an accomplished instrumental ensemble.

The following dawn brought a third day of sunshine, making this the only scientific event in Padua among the many attended by your correspondent that was not irrigated by sheets of rain descending from the grey Venetian heavens. The two remaining Symposia were held in the more austere clinical setting of the Aula Morgagni at the University Hospital which, if lacking the lustrous Renaissance decorations of the Aula Bo, had the advantage of adjacent functional toilets. Unfortunately, Galileo and his associates had omitted to install these facilities in the earlier building, and those in need had to embark on a long and intricate journey in search of relief that took up the entire coffee-beak. One had to admire the way most of the locals, busily engaged in consuming delicious *biscotti* along with multiple cups of *espresso*, had learned to master their physiological functions.

Opening the Symposium *Enzymes in Gastrointestinal Diseases*, **Marina de Bernard, Padua**, devoted her talk to

Helicobacter pylori Cytotoxin A, its interaction with intracellular enzymes, and its role in gastric carcinogenesis. In a concise and beautifully illustrated presentation, she described its ability to localize with mitochondria, leading to channel formation and release of cytochrome c, and its multiple effects upon the immune system that are also associated with cytokine release.

She was followed by our generous host, **Mario Plebani, Padua**, who ambitiously set out to describe *Non-Invasive Approaches to the Diagnosis of Liver and Gastric Diseases*. The first topic occupied more than 75% of the time allocated to his lecture, and included a thorough evaluation of enzymes of matrix degradation, as well as simpler tests such as alpha-2 macroglobulin and haptoglobin in this scenario. Critically summarizing dozens of publications from his and other laboratories, he presented a meta-analysis of the data suggesting that the diagnostic failure rates were 18% for liver biopsy compared with only 5% for biochemical markers. Turning breathlessly to the second topic with seven minutes to go in a race against the clock, he illustrated the roles of the Urea Breath Test and measurements of Pepsinogens A and C as well as Gastrin-17 in this context. At the end of this brilliant *tour de force*, I was reminded of the boxer who was knocked out 9 seconds before the final bell, but he beat the bell and was so far ahead on points that he easily won the contest.

Daniela Basso, Padua continued with an account of the role in gastrointestinal carcinogenesis of *DNA-Repairing Enzymes Gene Polymorphism and Mitochondrial DNA Mutations*, in the course of which she reviewed all the major pathways leading to colorectal cancer. The cycle of local expertise was temporarily interrupted by **Holger Kalthoff, Kiel, Germany**, who illustrated the *Role of Protein Kinases in Pancreatic Carcinogenesis*, commencing with the reminder that this was now the fourth most common cause of death from cancer in his home country. His lecture focused upon three specific classes: Tyrosine-specific protein kinases; the CAMK family, with special emphasis on Protein kinase D; and the Casein kinase-1 family. But Padua had the final word in the form of a presentation on *Enzymes in Faeces: Useful Markers of Chronic Bowel Disease* given by **Imerio Angriman**. Few would have expected many rewards from this descent into the lower depths of the GI tract, but Dr Angriman taught us otherwise, and made a convincing case for the role of fecal lactoferrin in discriminating between Crohn's Disease and Ulcerative Colitis on the one hand and other forms of inflammatory bowel disease on the other. I was reminded of the old Yorkshire proverb: *Where there is muck there is money*, although here the context is agricultural (the fertilizing value of animal excrement) rather than diagnostic.

A leisurely lunch at a typical local restaurant was followed by the Final Symposium: *Enzymes in Neoplastic Diseases*, to which Padua contributed the first two speakers. **Paolo Bernardo** treated us to a scholarly account of *Apoptotic*

Pathways and Caspases in Cancer, and **Spiridione Garbisa** spoke on *Matrix Proteases, Green Tea, and Hypericum – Biomedical Research Catches up with Folk Medicine*. There is persuasive evidence from the current literature that, with the exception of the epigallocatechin derivatives of green tea, few of these natural compounds are absorbed by humans in concentrations likely to achieve pharmacological efficacy, but data exhibited by Dr Garbisa contradicting this view seemed to be quite convincing. We can only hope that these controversial results are soon confirmed.

Like the invasion of Rome by the Huns, the Vandals and the Visigoths, the bright lights of Padua were finally extinguished by Anglo-Saxon hordes, but on this occasion invading from the West. *Kallikrein Enzymes as Biomarkers for Cancer* offered an opportunity to **Eleftherios P Diamandis**, *Toronto, Canada*, to review the outstanding work of his group in the identification of these enzymes and their genomic organization, as well as their contributions to clinical medicine. This was very serious stuff. Evidently, Dr Diamandis agreed, because he exhibited little of the brilliant humour for which he is renowned. **Catherine M Sturgeon**, *Edinburgh, Scotland*, followed with *Standardization and Quality Assessment of PSA Assays*. I debated whether or not to miss this talk, since nothing bores me more than someone trotting out the old predictable formulae for standardization and QC of

this, that, or the other. In the end, I was glad that I remained, for the lucidity, coherence, and sheer common sense behind her lecture made up for the over-familiarity with concepts like bias, imprecision, and calibration error. It was left to **Daniel W Chan**, *Baltimore, USA*, to bring the Conference to a close by describing the *Discovery and Validation of Clinical Proteomic Biomarkers as Related to Enzymes*, focusing upon new enzymes and their diagnostic assays.

There was ample opportunity for interaction between audience and speakers during the scheduled Discussion Periods, as well as at the end of some of the individual lectures. Generally, the intensity of the questions and comments by the registrants, approaching 200 in number, evinced a high degree of interest in the material presented. There should be a warm reception for the Special Issue of *Clinica Chimica Acta* featuring full papers on most of these presentations that will be published next year with **Mario Plebani** as Guest Editor. Whether this represents a reward for his efforts or an added layer of responsibility, I leave the reader to surmise, but in so far as it is a reward of any kind at all, the warm appreciation of all who came to this Conference, as well as the knowledge, inspiration, and happy memories that they will take with them, can be firmly assured.

DAVID M GOLDBERG

KALLIKREIN MEETING

2nd INTERNATIONAL SYMPOSIUM ON KALLIREINS AND KALLIKREIN-RELATED PEPTIDES

SANTORINI, GREECE, OCTOBER 16 to 18, 2007

The above meeting, organized by the International Kallikrein Society, with co-sponsorship by the International Society of Enzymology together with the Hellenic Anticancer Institute and the Frey-Werle Foundation, will bring together an eminent group of scientists from around the globe. The keynote speaker will be Dr. Judith Clements of Australia. Other confirmed speakers include Eleftherios Diamandis and Morley Hollenberg from Canada, Wolfram Bode and Manfred Schmitt from Germany, and David Deperthes from Switzerland. In addition to basic science and molecular biology, the focus will be on applications of this knowledge to diagnostic and therapeutic aspects of human disease. Registrants are encouraged to offer abstracts for both short oral and poster presentations. Full details may be found on the IKS website: www.kallikrein-society.org