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EXPERT OPINION

Introduction for the Fourth International Symposium on Thymosins in Health and Disease

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The Fourth International Symposium on Thymosins in Health and Disease brought together many of the leading scientists, clinicians and thought-leaders from the United States, Israel, Europe, China and Japan to discuss the latest advances and clinical applications of the thymosins in both basic and clinical areas. The symposium, held in Rome, Italy, on October 23 – 25, 2014, was sponsored by The George Washington University and the University of Rome 'Tor Vergata.'

Keywords: disease, health, meeting, thymosin

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The four plenary sessions were devoted to advances in basic research and translational advances in the areas of immune deficiency diseases, AIDS, infectious diseases, cancer, wound healing, and in the treatment of dry eye, severe sepsis, cardiovascular diseases, hepatitis B and neurological pathologies, including trauma, stroke and peripheral neuropathy.

Michael Chopp, Ph.D., the Scientific Director of the Henry Ford Neuroscience Institute in Detroit [1] and Barbara Ensoli, M.D., Ph.D., the Director of the National AIDS Center, Instituto Superiore di Sanita in Rome, gave keynote lectures and were the co-recipients of the 2014 Abraham White Distinguished Science Award [2]. Guido Rasi, M.D., the Executive Director of the European Medicines Agency, was the 2014 recipient of the Abraham White Lifetime Public Service Award [3].

Michael Chopp was honored for his pioneering studies and scientific contributions, which have significantly advanced our understanding of the role of thymosin β_4 in the treatment of a number of neurological diseases [1]. Studies from the laboratories of Dr. Chopp and his colleagues at the Henry Ford Hospital have shown that thymosin β_4 improves neurological function after stroke, traumatic brain injury, multiple sclerosis and diabetic peripheral neuropathy in adult rats. His studies have provided definite evidence that the improvement in neurological function derives, at least in part, by increasing the formation of protective myelin around nerve fibers in the CNS and peripheral nervous system.

Barbara Ensoli was honored for her pioneering studies and scientific contributions, which have advanced our understanding of the role of the HIV-1 Tat protein antigen in the development of both preventive and therapeutic HIV vaccines [2]. The use of the HIV-1 Tat protein as a candidate vaccine antigen represents a radically different approach to creating a vaccine against HIV-1 since it is based on the use of a regulatory protein produced very early after HIV infection, instead of the use of envelope proteins as most other HIV AIDS vaccines tested in the clinic to date do. 'The Italian AIDS vaccine,' as it has been termed, has successfully been tested in preclinical studies and has been found to be safe and immunogenic in Phase I clinical studies, and is being currently tested in Phase II therapeutic studies in Italy in subjects under antiretroviral therapy.

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Guido Rasi was honored for his lifetime of scientific and medical accomplishments in advancing the development of new preclinical models in oncology, including the use of novel combinations of chemo-immunotherapeutic approaches and nanosystem drug delivery, and as the Executive Director of the European Medicines Agency. He received his award at the banquet of the meeting and delivered a keynote address entitled 'Innovate therapies for the 3rd millennium.'

The conference scientific summary

The papers included in the volume of these proceedings highlight the significant progress that has occurred in our understanding the role of thymosin peptides in health and disease. The papers summarize the most recent advances in basic research, including mechanisms of action, which have provided the scientific foundation for translational studies with thymosin α_1 and thymosin β_4. In this volume, there are several reports describing novel formulations, diagnostic advances, as well as characterization of a synthetic thymosin β_4 fragment with antimicrobial properties isolated from the sea urchin *Paracentrotus lividus*.

Plenary session I focused on the chemical and pleiotropic effects of thymosin α_1 and thymosin β_4 including historical reviews and chemical techniques to label and identify thymosin peptides. Paracentrin I, a synthetic antimicrobial peptide fragment of a β-thymosin, was shown to interfere with staphylococcal and *Pseudomonas aeruginosa* biofilm formation. In studies on $T\alpha_1$, it was reported that this peptide also triggers TLR in dendritic cells.

Plenary session II was devoted to reports on the mechanism of action of $T\alpha_1$ and $T\beta_4$ in a number of cellular assays. It was reported that $T\alpha_1$ stimulates complement receptor-mediated phagocytosis in mature macrophages utilizing the N-terminal region. In studies with $T\beta_4$, it was reported that $T\beta_4$-coated monofilm scaffolds could repair damaged heart tissue and that $T\beta_4$ could reduce lung fibrosis. Similar beneficial results were reported with $T\beta_4$ using a kidney animal model.

Plenary session III focused on the role of synthetic thymosin β_4 in providing protection in cardiovascular disease and in treating patients with neurotrophic keratitis and dry eye. Papers were also presented using a gene transplant model demonstrating that $T\beta_4$ controlled blood vessel growth and maturation. In an interesting study of $T\beta_4$, using a $T\beta_4$ KO mouse model, it was reported that this peptide regulates titin splicing. In other reports using novel prothymosin peptides, it was found that a prothymosin hexapeptide could cross the blood–brain barrier and repair the brain following an ischemic event in mice. Another prothymosin variant was found to suppress HIV *in vitro* via induction of Type I IFN induction.

Plenary session IV looked at both *in vitro* and *in vivo* clinical applications of a number of thymosin peptides. The role of $T\alpha_1$ in preclinical models of melanoma and sepsis provide new insights into clinical opportunities for this drug as did a study of $T\beta_4$ in a mouse model of pulmonary hypertension. Other reports provided data on ongoing late-stage clinical trials in China with $T\alpha_1$ in HBV and in hepatocellular carcinoma. In a study looking at the active sites of $T\beta_4$, it was reported that a C-terminal tetrapeptide was active in both cardiac cell migration and repair.

The increasing number of synthetic thymosin peptides and analogs available has significantly accelerated animal model experimentation in the field and has helped researchers to consider novel clinical applications. These Proceedings should be of keen interest to both basic and clinical scientists, as well as pharmacologists, immunologists, biochemists and cell biologists with interests in the use of thymosin peptides to modulate immune responses. It should also be of special interest to physicians and other health-care workers studying the clinical applications of the thymosins in both health and disease.

We would like to thank the program committee: Anna Teresa Palamara, Francesca Pica, Paola Sinabaldi-Vallebona, Gabe Sosne, Cartasio Favalli, Roberto Camerini, Paul Riley, Ewald Hannappel, Hynda Kleinman, Luigina Romani, Cynthia Tuthill, Deepak Srivastava and Hiroshi Ueda for their help in planning this important scientific symposium. We would also like to acknowledge the editorial staff of Expert Opinion for their support in editing and publishing this issue.

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