



## Introduction to the Special Issue on Non-oncological Uses of Hyperthermia

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## Introduction to the Special Issue on Non-oncological Uses of Hyperthermia

In September of 2008, I had the honour of organising the twenty-fifth annual meeting of the Japanese Society for Thermal Medicine (JSTM) in Nagoya, Japan. The main theme of our meeting was 'Hyperthermia is still with us in the midst of expanding medical applications'. Because of long-standing and growing interest in Japan in the use of heat treatment for diseases in addition to cancer, evidence of the 'expanding medical applications' was especially apparent at this meeting. Indeed, we had a large focus on non-oncological applications of hyperthermia. For example, one of the symposiums was entitled 'Molecular chaperones and lifestyle-related illness'. Also, the protective effect of heat shock proteins on neurodegenerative diseases was presented in a special lecture. Several presentations on the effects of hyperthermia on the immune response were included during a highly interactive workshop with diverse topics. Since Japan is one of several countries witnessing a significant increase in diabetes, our meeting also included research into the effects of hyperthermia and heat shock proteins in the progression of this disease.

In this special issue of the *International Journal of Hyperthermia* we decided to highlight this rapidly growing field of research in Japan, in the hope of increasing the awareness of others of the exciting new research being done into non-oncological applications of hyperthermia. In addition, we asked some members of the Biomedical Society for Stress Response (BSSR), a Japanese branch of Cell Stress Society International (CSSI), to contribute to this special issue. This special issue contains both original and review articles on a variety of emerging fields of research.

Personally, I am very interested in changing paradigms associated with the use of hyperthermia that we are witnessing in Japan. Most importantly, although the temperatures used in oncological applications of hyperthermia have traditionally aimed for the heat shock range of approximately 43°C, it is of great interest that the majority of non-oncological applications are utilising milder temperatures (usually 39–41°C). As seen in several of the studies presented here, milder temperatures (around 40–41°C), which are not able to directly kill most cells, have been shown to have some

therapeutic effects on several diseases such as diabetes and osteoarthritis, and are showing some benefit in oncological applications as well. These beneficial effects are considered by many to be attributed, at least in part, to the thermal activation of various cells of the immune response.

There are also new directions in the role of heat shock proteins (HSPs) in the processes that regulate a variety of diseases including cancer, and several papers in this special issue are concerned with this topic. Preventing cellular damage as a result of micro-environmental stresses in organisms is critical to survival, and multiple forms of protective mechanisms against stresses within the cells have emerged during evolution. The heat shock response is one such protective mechanism used to help survive changes in environmental conditions. Heat shock proteins induced by various environmental stresses are known to function as molecular chaperones within the cells to ensure protein homeostasis and to protect cells from deleterious and proteotoxic stresses. Moderate overexpression of HSPs by mild temperature or by non-toxic chemical compounds has been shown to have beneficial effects on various pathological states, such as stress ulcers and ischaemia-induced tissue injuries, as well as inherited diseases associated with protein misfolding and protein aggregation. Recent reports indicate that HSPs work not only within the cells but also outside of cells. Extracellular HSPs are considered to play a role to stimulate the innate immune system as a danger signal or a warning signal. Thus, the activation or modulation of heat shock response might be applicable for the prevention and treatment of not only cancer but also other diseases, and researchers in Japan are also very interested in this goal.

In summary, I believe it would be a great delight to all of us working in the field of hyperthermia in Japan if this special issue contributes to a world-wide expansion of interest in, and understanding of, the potential uses of hyperthermia and heat shock proteins in the treatment of multiple diseases in addition to cancer.

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