

□短報(依頼稿)□

Adiponectin modulators: New approach for scaling up noncommunicable diseases (NCDs) prevention and management ?

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I. Burden of Noncommunicable Diseases in the World and Eastern Asia

Noncommunicable diseases (NCDs), including cancer, cardiovascular, metabolic syndrome, diabetes and other metabolic diseases have become a major public health problem in many countries. They are the leading cause of death worldwide^{1,2}. A recent NCDs world report from the World Health Organization (WHO) suggests that without proper investment to counter those diseases, 15 million people will continue to die annually from NCDs, between the age 30 and 70 years³. On the other hand, metabolic risk factors such as hypercholesterolemia or hyperlipidemia, high level of fasting blood glucose, high blood pressure and obesity which cause metabolic syndrome, diabetes, hypertension, atherosclerosis, arteriosclerosis, and other NCDs are closely related to reduced level of circulating adiponectin (ADN)⁴⁻⁷. In Eastern Asian countries, NCDs are also becoming public health issues. Recently, NCDs morbidity and mortality have increased tremendously in China, Korea and Japan mainly due to sedentary lifestyle, and increasing fat and protein intake as well. In Korea, the proportion of mortality from major NCDs increased from 39.4% in 1984 to 56% in 2011, whereas in China 80% of all deaths in 2005 were caused by NCDs⁸.

The global burden of diabetes is also getting worrisome. Globally, the prevalence of type 2 diabetes (T2D), one of most common NCDs, has been increasing and the International Diabetes Federation predicted that the number of diabetics will increase from 366 million to 552 million by the year 2030⁹. It has been reported that Asia accounts for

60% of the world diabetic population, whereas the disease prevalence keeps increasing in Japan with an estimated number of patients reaching approximately 9 million in 2007¹⁰. In the following lines, we provide insights on different approaches that are more likely to prevent and, possibly, cure NCDs with a particular focus on adiponectin modulators. We also provide an outline on IUHW contribution in capacity building for a better DBT management.

II. Prospects to Reduce NCDs Burden and Enhance Cardiometabolic Health in Communities

Several approaches have been proposed to reduce the burden of NCDs, mainly tobacco smoking ban in public places, cessation of harmful alcohol consumption, healthy diet and physical activity. These approaches have helped to save many lives as they allow not only to prevent NCDs development in individuals at high risk, but also to improve the health of NCD patients. Recent advances in Regenerative Medicine (RM) have revolutionized NCDs treatment. RM has initially focused on tissue engineering to replace damaged tissues and organs with the use cells and biomaterials. For instance, the use of stem cells such as induced pluripotent stem (iPS) cells to produce organ tissues is one of RM procedures that have brought a new hope for the treatment of a number of incurable conditions that have been poorly managed with conventional medical procedures. However, this discipline has recently expanded into other types of translational medicine that modulate the human body's own endogenous or physiological processes, either to prevent tissue and function damage or repair, re-

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generate the damaged tissue or function¹¹). For example, the use of immunomodulators that provide outstanding outcomes is believed to be a promising preventive and therapeutic procedure for NCDs. It is well established that most cardio-metabolic diseases are associated with circulating adiponectin (ADN), a hormone produced by fat cells (adipocytes). ADN is reported to have salutary health effects, and it has been proposed as a new approach for NCDs treatment.

In the scientific literature, there are studies that showed a strong association between circulating ADN and NCDs, suggesting that increasing ADN level in subjects at risk or NCD patients may improve their health¹²⁻¹⁴). An experimental study conducted by a team of Canadian researchers showed that ADN gene therapy markedly ameliorated diet-induced metabolic perturbations such as high fat and high blood glucose levels¹⁵). This finding supports the assumption that ADN, if produced in laboratory or synthesized *in vivo* could serve as therapeutic approach for common cardiovascular and metabolic diseases, including diabetes.

Nowadays, many specialists in the field of NCDs have been searching for novel drugs and bioactive compounds that could modulate ADN production or mimic its function, given the difficulty to synthesize ADN in laboratory. Although clinical trials on AdipoR agonists are still scarce, a number of *in vitro* and animal studies are available in the literature. These include studies on Adiporon^{16, 17}), an adiponectin receptors 1 and 2 (AdipoR1, AdipoR2) agonist that has shown promising results. Additionally, a few studies suggested that omega-3 polyunsaturated fatty acids (PUFA) such as EPA and DHA induced an increase in serum ADN level; but the gain was low (less than 1.1-fold), and no significant difference was observed when compared to the control (placebo) group^{18, 19}).

Our recent collaborative work showed that dietary supplementation with Tosa-SBM, alga-derived biomaterial from Kochi prefecture in Japan, up regulated ADN production, inducing a 2 to 3-fold increase in ADN level after a

four-week intake of the Tosa-SBM supplement, with no adverse effect reported, whereas no change in ADN level was observed in controls. It also improved cardiometabolic and BMI profiles^{12, 20, 21}). Tosa-SBM is rich in ulvans that are known to have anti-inflammatory property²²); and, considering its good safety profile, it is a promising natural ADN modulator with a potential to be used as NCDs preventive agent for community health interventions and, possibly, as an adjuvant therapeutic agent in patients.

III. Scaling Up NCDs Prevention and Management

NCDs are posing a serious health and economic burden worldwide; thus there is a necessity to elaborate novel strategies to reduce their prevalence and improve disease management. The discovery of natural immunomodulators such as ADN modulators is a step towards tackling the NCDs burden in communities, thanks to their good safety profile. In addition to NCDs research funding for the discovery of new drugs and other remedies, increasing the number of health promotion facilities (fitness and sports centers, healthy diet and lifestyle) and capacity building of health care providers in NCDs management would contribute to reducing NCDs prevalence and the related economic burden.

For instance, the IUHW Sanno Hospital (Tokyo) initiative that consists of organizing seminars aimed at fostering mutual understanding between healthcare providers involved in diabetes management and improving their knowledge on diabetes and management²³). It is noteworthy to organize a series of seminars where speakers from different specialties share about their experiences in caring for diabetic patients and suggestions for better disease management. Such initiatives allow health professionals to have a good understanding of the disease and work together as a team to improve patient care. Expanding such an educational program may enhance diabetes management on local and even regional level. Furthermore, prefectural and city governments should promote the implementation of similar and

adapted programs at community level. Then, community members will acquire basic knowledge on most prevalent NCDs and foster necessary family supportive care for affected members.

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