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Editorial

The Potential Power of Stress

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As one of the greatest advances in molecular and cellular biology, Yamanaka's group demonstrated a method for creating induced pluripotent stem cells in 2006 [1]. This technique provides differentiated cells with an embryonic ability to turn into almost any cell type in the mammalian body by introducing four transcription factors. For this work, Dr. Yamanaka won the Nobel Prize for medicine. His method requiring genetic manipulation, however, carries a potential risk of triggering the development of cancer.

Seven years later the work by Yamanaka's group, two studies published in *Nature* strikingly advanced the method of inducing pluripotency [2,3]. Very recently, Obokata and colleagues discovered that mammalian somatic cells can be reprogrammed into pluripotent cells without the need for nuclear transfer or genetic manipulation. This conversion process was subsequently named stimulus-triggered acquisition of pluripotency (STAP). Surprisingly, STAP cells are created merely by exposing the cells to sublethal (strong external) stimuli, such as that immersed in a transient low-pH medium. The surviving STAP cells exhibit various characteristics that resemble those of embryonic stem cells. Although it is unknown whether the methodology used to create STAP cells is truly reproducible and thus can be applied to human somatic cells, these scientific breakthroughs have great implications for the field of regenerative medicine.

The remarkable findings of Obokata, et al [3]. are reminiscent of the stress response model developed by Dr. Hans Selye, a famous pioneering endocrinologist who investigated the effects of stress on the mammalian body. Selye published his discovery in *Nature* in 1936 under the title "A syndrome produced by diverse nocuous agents" [4]. Based on this work, the stress response constitutes the body's reaction to any demand made upon it and can subsequently induce disease via the overproduction of adrenal hormones and/or stimulation of other pathways [4-6]. There is considerable interest in the stress response, and a growing body of research has extended the findings of Selye's study to a variety of scientific and social areas in association with the creation of new academic fields called "psychoneuroendocrinology" and "psychoneuroimmunology" [7,8]. The extensive interactions observed between psychological and behavioral factors and various biological mechanisms, such as those underlying the nervous, endocrine and immune systems, have been explored in relation to wellness, illness and disease. Such interactions have been considerably investigated at the workplace in which we spend almost one third of our life [9,10]. Moreover, the role of stress has been evaluated with respect to genetic alterations. We previously reported that physical factors, such as working long hours, and psychological factors, such as stressful life events and mood changes, are associated with oxidative DNA damage in peripheral leukocytes and/or urine [11,12]. Depressive patients showed higher level of leukocyte oxidative DNA damage than healthy controls [13]. Seventy-eight years after the publication of Selye's work, the same journal has given the stress response special attention with respect to somatic cell reprogramming into pluripotent cells [2,3].

Stress is inevitable in daily life and is often considered to be a health hazard. However, stress is not necessarily harmful. Stressful experiences play an especially prominent role in promoting adaptive responses [4-6]. Whether stress on a given organism results in disease or an increase in energy and achievement depends on how the body interprets the stressful stimuli. Additionally, the perception that stress has adverse effects on health has led to the hypothesis that psychological stress acts synergistically based on the degree of stress, thus predicting an increased risk of premature death [14]. In other words, cognitive awareness is beneficial for altering a negative stress state to a more positive stress state. Stress thus enhances our ability to adapt both physically and psychologically to environmental and/or internal demands that we can handle [4-6]. Selye called stress "the spice of life" as a vital part of human existence. Obokata and coworkers highlight and advance this positive aspect of stress, particularly regarding the concept of survival of the fittest from the molecular and cellular perspective of the STAP phenomenon [2.3]. This topic may lead to a discussion of Darwin's theory of evolution, which demonstrated the model of ultimate adaptation to extreme environmental changes [15]. Selye also described stress as the "The great laws of nature that regulate the defenses of living beings against stress of any kind are essentially the same at all levels of life, from individual cells to entire complex human organisms and societies" [16]. Stress may bring about extremely powerful developmental changes if the organism is able to adapt positively and escape from lethal situations. It is therefore very important to perceive stress as "the spice of life" in order to enhance adaptive resources to enrich one's life. Further examinations using modern biological technology are needed to explore stress, including psychological aspects,-related adaptive abilities and mechanisms.

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