

Rejuvenating the Skin While Protecting DNA Integrity

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Abstract

Induced by the exposure to environmental agents and inner factors, damage accumulates inside cells with the passing of the years. Once it is agreed that lifespan is directly linked to the ability to protect the genetic code and avoid cellular damage persistence, DNA integrity is crucial for any organism. Considering this purpose, the Forkhead box (FOX) agents represent an essential family of transcriptional factors that regulate the expression of genes implicated in cellular protection and longevity. Included in the FOXO subclass, FOXO3a can indirectly induce programmed cellular death when DNA errors are too severe to be fixed and cell-cycle arrest if they can be repaired and it can also increase gene expression linked to this amending process. Thus FOXO3a is important for genetic integrity and a decrease in its activity would lead to damage accumulation and reduced cellular functionality, which actually occurs during ageing.

Our company proposes a cosmetic solution to preserve DNA integrity. Juvefoxo™ peptide is an innovative ingredient capable of imitating FOXO3a activity, reducing DNA damage accumulation. It is not only proven to raise the activity of the FOXO3a responsive elements but also the DNA-repair pathways themselves. Additionally, it protects cells from UV exposure and pollutants, highly increasing their viability and decreasing the number of senescent cells by 64.5%, which implies a cellular rejuvenation of 11 years. *In vivo*, it reduced the UV-induced errors (CPDs) by 16.6% (at 2% peptide solution), involving a repairing effect. Thus, Juvefoxo™ peptide helps cells remain unimpaired for longer.

Introduction

The term genome is not unfamiliar nowadays where information spreads fast and widely, being properly understood as an extensively-used natural storage system for the entire hereditary information of an organism. Deoxyribonucleic Acid (DNA) is an essential part of this vital puzzle and it contains informational elements that encode the genetic instructions for the develop-

ment and functioning of almost all organisms. DNA consists of two long chains of nucleotides twisted into a double helix and joined by hydrogen bonds between the complementary bases adenine and thymine or cytosine and guanine. The sequence of nucleotides determines the hereditary features of each individual and the preservation of its integrity is indispensable for life and survival.

Inconveniently, keeping the genetic information free from mutations is a particularly demanding task as DNA is a chemical entity subject to constant assaults and errors induced by different factors⁽¹⁻²⁾. Apart from its intrinsic biochemical instability, DNA strands suffer the continuous influence of endogenous and exogenous genotoxic agents (oxidative stress, environmental conditions, etc.) and mistakes during its replication⁽¹⁻²⁾. Specifically, it is estimated that an individual cell can experience up to one million DNA changes per day⁽³⁾.

Even though genetic mutations can imply evolutionary benefits, sometimes they can also be deeply unfavourable and generate cellular damage or even death, with the consequent effects at a macroscopic level. In order to preserve DNA from keeping these errors, cellular cycle checkpoints are induced to arrest the cellular cycle when the damage is detected so that it can be repaired before it is propagated to daughter cells⁽⁴⁾. The DNA damage response leads to the induction of transcription programmes, enhancement of DNA-repair pathways and initiation of cellular death (apoptosis) when the level of injury is too severe⁽⁵⁾. Failing to repair such DNA lesions may result in severe injuries involved in a variety of genetically inherited disorders and ageing in humans^(2, 5-6). As with any other organ, the skin suffers the consequences which involve a negative effect on its functionality, properties and its overall appearance, looking noticeably older.

DNA damage and instability can be caused by a range of sources, including external reasons such as UV exposure, pollu-