

Letter to the Editor

Apoptotic gene therapy in the interdigital web

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Dear Editor,

Apoptosis plays an essential role in sculpturing the body during the embryo development.¹ The formation of the interdigital web in chicks, as well as in ducks, involves a time and space specific form of apoptosis, where a crucial role is played by the *msx* gene,² *BMP-2/4*,³ and tissue transglutaminase.⁴ In mammals there is evidence of involvements of caspases.^{5,6} However, in the absence of *apaf-1*, cell death still occurs, but with a significant delay, and in the form of necrotic death,⁷ suggesting that the interdigital web death stimuli are incompatible with life, resulting in unsustainable free radical damage.

We have identified a new essential molecular pathway that can cause persistence of the interdigital web.

In order to identify the defect at the molecular level, we screened for several genes in keratinocytes cultured from an interdigital web biopsy. In addition to the involvement of caspases, *apaf-1*, *msx*, *BMP-2/4*, and tissue transglutaminase, as outlined above, we identified the expression of a novel unknown protein band. We then established a collaboration with professor Sum Ting Wong, a fugitive from the North Korean University Hu Yu Hai Ding, currently in Rome (Italy). By performing a differential protein labeling on line with quadruple eptapole massive spectroscopy we identified this extremely faint spot. This was identified as the new protein Wai So Dim (WSD). WSD is a transcription factor belonging to the p53 family that controls the expression of the ER protein Scrocin,⁸ and thus regulates apoptosis. On the other hand, WSD also transcribes *p16INK4a*^{9,10} and *Bmi1*,¹¹ suggesting its involvement in senescence. Indeed, we further demonstrated that WSD regulates the Rb-E2F senescence pathway.¹²

Based on new, patented biological effects of WSD we found two biotech companies, Gene-Italia (Italy) dedicated to the development of interdigital web gene therapy and Ai-Bang-Mai-Ni (Japan) for orthopedic applications. Gene-Italia has successfully performed adult local gene gun induction of WSD, using a cassette to eventually eliminate its expression,¹³ Figure 1. The recreation of an extensive interdigital web in a young male led to reduction from 125 to 62 s, the time required to complete the 100 m Freestyle (Olympic rules). In addition to success in swimming competitions, the volunteer has now been involved with sport advertisement companies.

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Figure 1 Re-creation of the interdigital web after WSD gene gun in a nonprofessional swimmer, now regional champion (Ohmy God Ih Swimfast). We thank Arena Italia spa thanks to Enzo Guida, Brand Manager Arena Italia spa; www.arenaitalia.it; the photo was made by LSD, Lowe Pirella Agency, and Umberto Casagrande, Art Direction and Creativity Director

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