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GUANINE DEAMINASE (GDA) – FROM METABOLISM TO SKIN AGING, PIGMENTATION AND IMMUNE DEFENSE

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Guanine deaminase (also known as guanase;) is a zinc-dependent enzyme that converts guanine to xanthine, marking the first dedicated step in breaking down purines. It is one of another deaminase group enzyme, as adenosine deaminase and cytidine deaminase. For a long time, guanine deaminase was used mainly as a blood marker for liver damage. However, new research shows that guanine deaminase does much more than liver chemistry – it also plays unexpected roles in skin aging, pigmentation, brain development, and immune system regulation. Guanine deaminase has been viewed as a liver-specific enzyme. But recent evidence reveals its presence and activity in other tissues, where it contributes to diverse biological processes.

The aim of this study is to summarize what is currently known about guanine deaminase's molecular actions, tissue-specific roles, and disease connections, with special focus on its newly discovered functions in skin photoaging, melanin production, nervous system development, and immune-related disorders. We analyzed peer-reviewed studies from hepatology, dermatology, neuroscience, and immunology. Data came from enzymatic assays, cell and animal models, human tissue samples, phylogenetic comparisons, and structural biology studies.

The old view of guanine deaminase as a passive liver marker has changed. In the skin, guanine deaminase is highly active in seborrheic keratosis and melasma. It drives ultraviolet-induced aging of keratinocytes by producing uric acid, which causes oxidative stress and deoxyribonucleic acid damage. Moreover, skin cells that overexpress guanine deaminase release uric acid, which nearby pigment cells take up through the adenosine triphosphate-binding cassette subfamily G member 2 / PDZ domain containing 1-dependent transport and urate transporter 1-mediated uptake. This activates the p38 mitogen-activated protein kinase signaling pathway and increases melanin production via microphthalmia-associated transcription factor, tyrosinase, stem cell factor, and basic fibroblast growth factor. In the brain, an alternative form of guanine deaminase called cytosolic PSD-95 interactor helps nerve cells grow dendritic branches by binding to postsynaptic density proteins and promoting microtubule assembly. Problems with guanine deaminase regulation have been linked to schizophrenia and autism spectrum disorder, partly through maternal antibodies. Structurally, guanine deaminase folds into a triosephosphate isomerase barrel fold, contains a single zinc ion, and uses two glutamate residues to shuttle protons. When guanine deaminase is missing, guanine builds up, disrupting deoxyribonucleic acid synthesis and causing cell death – effects that can be reversed by adding adenine or cytosine. Too much guanine deaminase, on the other hand, acts as a danger-associated molecular pattern and can become an autoantigen in systemic scleroderma, where anti-guanine deaminase antibodies not only mark disease activity but also paradoxically increase enzyme function.

In conclusion, guanine deaminase is a clear example of how one enzyme can serve multiple roles – as a metabolic worker, a regulator of aging and pigmentation, a helper in brain development, and a player in immune defense. Its beneficial role in the brain contrasts with its harmful effects in skin aging and autoimmunity, making guanine deaminase an attractive target for future treatments. Potential applications include therapies for seborrheic keratosis, hyperpigmentation disorders, and cognitive diseases with abnormal nerve cell branching. Understanding how different forms of guanine deaminase are regulated in different tissues, and how guanine deaminase evolved from bacteria to humans, will be key to designing targeted drugs.