Glycodelin – Newer perceptions

Sir,

Glycodelin (Gd), a lipocalin protein, is a potential paracrine regulator with significant effects on immune cells, apoptosis, reproduction, cell adhesion, differentiation, and cancer. Gd is known to have isoforms, namely, GdS (found in the seminal plasma), GdA, and GdF (produced by the fallopian tube). GdS suppresses albumin-induced cholesterol loss and maintains the spermatozoa in an uncapacitated state before they enter into the cervical canal where GdS is removed. GdA and GdF inhibit the binding of spermatozoa to the zona pellucida. While GdA may protect the spermatozoa from a maternal immune attack by its immunosuppressive activity [blocking the GdA–sperm receptor complex fucosyltransferase-5 (FUT5)], GdF suppresses the premature progesterone-induced acrosome reaction. GdA sensitizes spermatozoa in a glycosylation-specific manner through the activation of the adenylyl cyclase/PKA pathway, suppression of extracellular signal-regulated kinase (ERK) activation, and up-regulation of the zona pellucida-induced calcium influx.[1] The cumulus oophorus cells transform GdA and GdF to GdC, which in turn removes the spermatozoa–zona binding inhibitory Gd isoforms and enhances the zona binding capacity of spermatozoa.

Levonorgestrel taken before the LH surge is known to prematurely increase serum and intrauterine concentrations of Gd in the periovulatory phase. The role of Gd in fertility is elucidated by another study's finding where endometrial flushing fluid Gd levels were higher in infertile women with abnormal tubes at day LH + 1 compared to fertile women (particularly in women conceiving after the following *in vitro* fertilization).[2]

GdA is abundant and ubiquitous in distribution in the first trimester and is known to significantly reduce the invasiveness of trophoblast via significantly reduced transcription of urokinase plasminogen activator (uPA) proteinase.[3] GdA inhibits the natural killer (NK) cell activity, T-cell proliferation, and chemotaxis of monocytes. Its physiological function is thought to mediate immunotolerance at the fetomaternal interface.

GdA increases the secretion of interleukin-6, interleukin-13, and granulocyte-macrophage colony-stimulating factor from NK cells. It shifts the Th1/Th2 ratio and induces immunological tolerance of dendritic cells and apoptosis of monocytes. Gd may mediate NF-κB inhibition, increase in Bad, Bax, and TNF-R1gene expression, reduction in Bcl-2A1 and a proliferation-inducing ligand (APRIL), and activation of caspases (8, 2, and 3) to execute programmed cell death. Conversely, reduction in the α2-6 sialylation of GdA impairs its T-cell apoptosis-inducing activities.[4]

Gd drives epithelial differentiation as exemplified by its more frequent expression in ovarian serous carcinoma and other well-differentiated carcinomas compared to the poorly differentiated. It also correlates with better survival. It is significantly lower in dysplastic lesions compared to normal squamous epithelium adjacent to CIN. In pregnancy, p16 expression inversely correlates with Gd as the preservation of Gd might be an epiphenomenon protecting dysplastic epithelia from HPV integration in the host cell DNA.[5] Gd is known to reduce breast cancer tumor growth *in vivo* owing to reduced expression of oncogenes and increased expression of tumor suppressor genes. Also, the down-regulation of the Gd gene causes endometriosis and progression of autoimmune disease.

There is an ever-expanding role of Gd in diagnostic and therapeutic applications in a variety of disorders that calls for awareness.

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REFERENCES

1. Chiu PC, Wong BS, Lee CL, Lam KK, Chung MK, Lee KF, *et al*. Zona pellucida-induced acrosome reaction in human spermatozoa is potentiated by glycodelin-A via down-regulation of extracellular signal-regulated kinases and up-regulation of zona pellucida-induced calcium influx. Hum Reprod 2010;25:2721-33.
2. Bentin-Ley U, Lindhard A, Ravn V, Islin H, Sørensen S. Glycodelin in endometrial flushing fluid and endometrial biopsies from infertile and fertile women. Eur J Obstet Gynecol Reprod Biol 2011;156:60-6.
3. Lam KK, Chiu PC, Chung MK, Lee CL, Lee KF, Koistinen R, *et al*. Glycodelin-A as a modulator of trophoblast invasion. Hum Reprod 2009;24:2093-103.
4. Lee CL, Lam KK, Koistinen H, Seppala M, Kurpisz M, Fernandez N, *et al*. Glycodelin-A as a paracrine regulator in early pregnancy. J Reprod Immunol 2011;90:29-34.
5. Zizzi A, Lucarini G, Stramazzotti D, Ciavattini A, Goteri G. Glycodelin and p16 expression in cervical intraepithelial neoplastic lesions: Differences between pregnant and non-pregnant patients. Ital J Anat Embryol 2010;115:83.

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