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Paths of evolution from normal to H-SIL cervical squamous epithelial cells: Computational simulations of clinical application

Javier Rodríguez, Signed Prieto, Catalina Correa, Leonardo Ramírez, Astrid Rubiano, Darío Domínguez and Marcela Mejía
Universidad Militar Nueva Granada, Colombia

Cervicovaginal cytology (CVC) evaluated by the current methodologies, such as the bethesda system, has low sensitivity and high false negative rates. One of the categories used for CVC diagnosis is ASCUS, which represents a nonspecific category under which intraepithelial lesions of low or high grade can be easily masked, evidentiating the importance of establishing an objective and reproducible method for determining the degree of differentiation of cervical squamous epithelial cells. In a previous work developed by Rodriguez et al., a new diagnostic method based on fractal geometry was developed to quantitatively differentiate normal cells from cells with low-grade lesions, based on the mathematical concept of intrinsic mathematical harmony (IMH) and variability of fractal dimension. In the present work, starting from fractal geometry and the concepts of IMH and cellular variability there were developed computational simulations of possible paths that could be taken by the squamous cervical cells from a normal stage to malignity. For this purpose, there were selected 10 normal cells, and 3 geometric variations of each one were made in the box counting space from normality to H-SIL, maintaining cellular IMH of each state, according to the developed diagnostic method. The simulations included relationships corresponding to the state called ASCUS, whose mathematical values can be normal or of L-SIL. The simulations obtained of possible paths from normality to ASCUS, L-SIL and H-SIL constitutes quantitative, objective and reproducible measures that evidence a fractal organization in the cellular architecture.

Biography

Javier Rodríguez is a physician from the Universidad Nacional de Colombia, founder and director of the Insight Group since 2001. He has more than 55 national and international original papers, with characterizations, diagnosis and predictions in different areas of medicine, such as fetal and adultcardiology, infectology, immunology, molecular biology, epidemics prediction, celular morphometry and psychology, as well as projects in physics. His investigations are based on the development of predictions from theories and laws of the theoretical physics. They can be applied to particular cases, avoiding the empirical method of trial and error.

grupoinsight2025@yahoo.es

M1/M2 macrophages: Copernican revolution in tumor immunology

Charles D. Mills
BioMedical Consultants

The purpose of immunology is simple. Cure or prevent disease. M1/M2 is useful because it is simple. M1/M2 describes the two major and opposing activities of macrophages. M1 activity inhibits cell proliferation and causes tissue damage while M2 activity promotes cell proliferation and tissue repair. Remark¬ably, the molecules primarily responsible for these "fight" (NO) or "fix" (ornithine) activities both arise from arginine, and via enzymatic pathways (iNOS and arginase) that down regulate each other. The names M1 and M2 were chosen because M1 and M2 macrophages promote Th1 and Th2 responses, respectively. Products of Th1 and Th2 responses (e.g., IFN-γ, IL-4) also down regulate M2 and M1activity, respectively. Thus, M1/M2 demonstrated the importance of innate immunity and how it is linked to adaptive immunity in a beautifully counterbalanced system. "Civilization" and increased longevity present new disease challenges such as cancer and atherosclerosis that do not display classical "foreign" antigens. And, these diseases are often associated with (or caused by) M1- or M2- type responses that were formerly useful for fighting infections, but now are inappropriate in our increasingly "germ-free" societies. In turn, there is considerable potential for modulating M1 or M2 Innate responses in modern diseases to achieve better health. Finally, since M1 and Th1 (or M2 and Th2) often work in concert to produce characteristic immune responses and disease pathologies, it is recommended that immune Type 1 or 2 (IT1, IT2) would be a simpler and unifying terminology going forward.

mills002@umn.edu