



Natural IgM antibodies: The orphaned molecules in immune surveillance[☆]

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Abstract

Natural IgM antibodies are typical victims of prejudices which originated in the mid 80 s. Over the years, these molecules were considered as the pariahs among the immune competent molecules and their characteristic properties, like low affinity, cross-reactivity and pentameric structure, were assessed as useless, difficult, nebulous, etc. Today, mainly based on a few scientists' persistent work and the key discoveries on innate immune recognition, natural IgM antibodies are "back on stage". Their role in the immune response against bacteria, viruses, fungi and possibly modified self-components as well as in therapy and diagnosis of malignancies is accepted. All the so far negatively judged features are seen in a different light, e.g. low affinity seems to be good for function and does not exclude specificity, and cross-reactivity is no longer judged as unspecific, but instead as a very economic way of immune recognition. And at last, with the use of natural IgM antibodies, a new field of tumor-specific targets has been encountered, the carbo-neo-epitopes. Therefore, by having learned from nature, the renaissance of natural IgM antibodies opens a new area of cancer therapeutics and diagnostics.

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1. Immune surveillance

More than 100 years ago, Paul Ehrlich discovered that animals could be immunized against diphtheria and that highly concentrated animal antisera could be successfully used to immunize children against diphtheria. Ehrlich assumed that molecules in sera of infected animals recognized and eliminated bacterial particles, and in 1897 he postulated the famous “side-chain-theory” [1,2]. Today we know that these “side chains” or “cast off” receptors

represent antibody molecules. It was Ehrlich who envisioned the creation of “magic bullets”, compounds that would have a specific attraction to disease-causing microorganisms. These magic bullets would seek out these organisms and destroy them, avoiding other organisms and having no harmful effects on the patients’ bodies [3]. It was Paul Ehrlich again who predicted that the immune system not only eliminates microbacterial invaders, but also represses the growth of carcinomas, by providing antibodies against malignant cells [3].

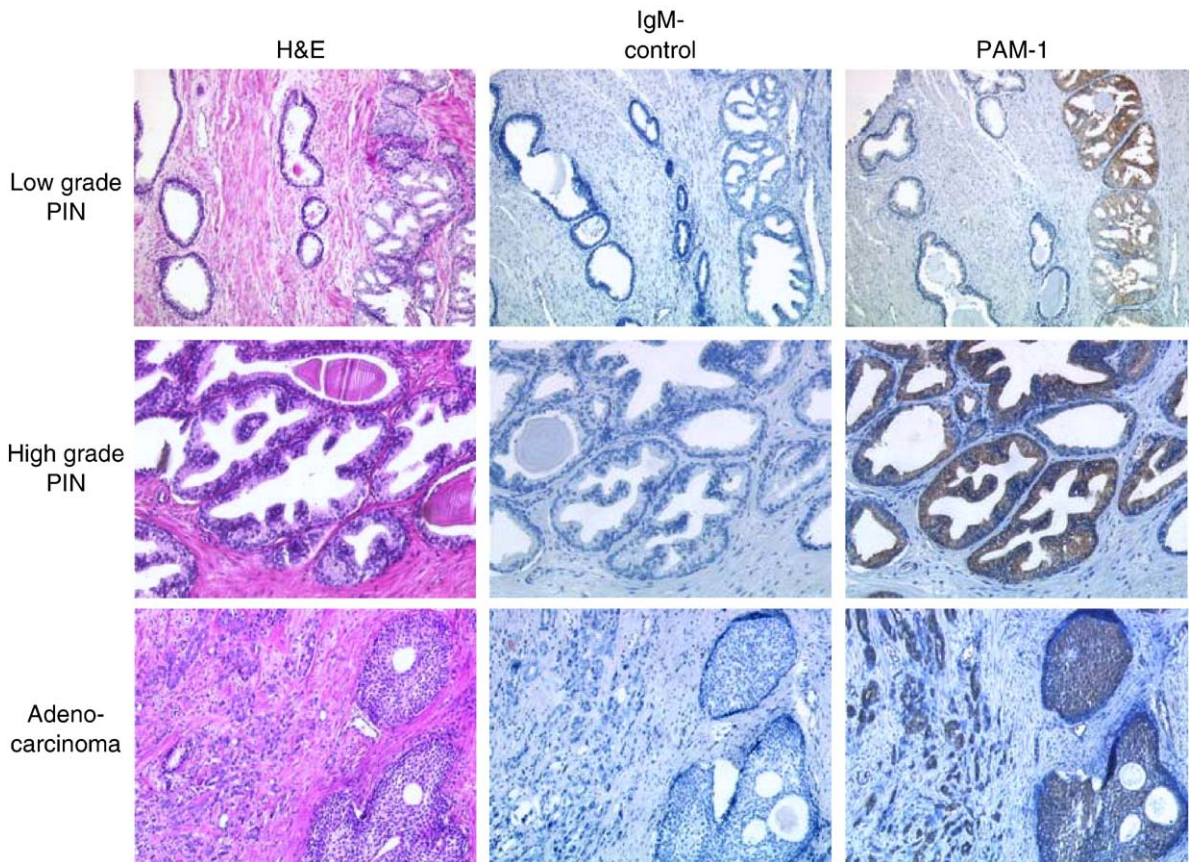


Fig. 1. Reactivity of IgM antibody with precancerous and cancerous tissue defined by immunohistochemistry. Paraffin sections were stained with hematoxylin–eosin (H&E), isotype matched control antibody as a negative control and antibody PAM-1 which was isolated from a patient with stomach carcinoma on low grade and high grade prostate intraepithelial neoplasia (PIN) and prostate adenocarcinoma. Original magnification: $\times 100$. Precancerous and cancerous cells are clearly stained positive with the human IgM antibody PAM-1.

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