The Universal Human Genome as reflected in Immunity

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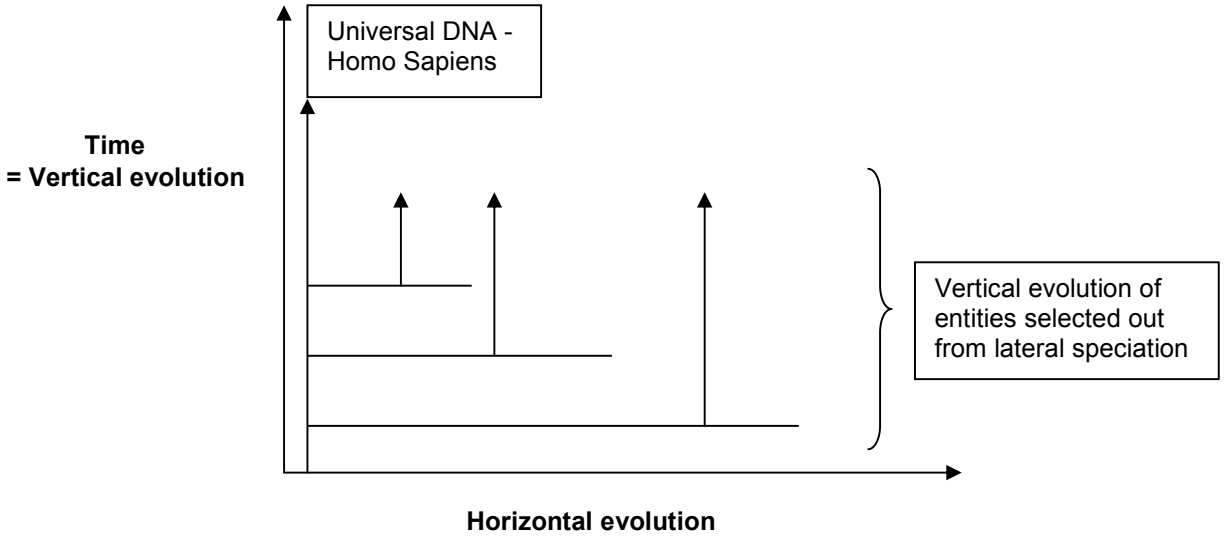
Introduction

It is my contention that the complete genotype representing the fully evolved human was in existence at the origin of life but in a fully suppressed state. Ongoing desuppression of appropriate segments of the genotype occurred in sequential environments. The intrinsic drive giving rise to the desuppression of sequential segments of the genome arose from changing environmental circumstances. The nature of the desuppression was therefore epigenetic. The process of sequential desuppression of the genome could also be seen to provide the template for the complex interlocking of the ecosystem.

Differing phenotypes reflect corresponding suppression or de-suppression of the genome. I have proposed that segments of the genome that are permanently suppressed may atrophy and cease to exist or cease to attain phenotypic expression in the specific organism (possible "junk" DNA or pseudo-genes). In this way the specific genome would ultimately differ from the "universal" one. Within a given level of speciation, mutation and natural selection would continue to occur. Thus lateral phenotypic change would give rise to species variation. These species would continue to evolve in a vertical manner in time, in parallel with the universal genome line. Two evolutionary processes can therefore be identified:

1. Epigenetic desuppression of segments of a comprehensive pre-existing genome. This I refer to as **vertical evolution**.
2. Lateral speciation due to mutation and natural selection. This I refer to as **horizontal evolution**.

This process is illustrated in the following diagram.



By implication one would expect the human genome to incorporate segments of the plant and animal genome spectrum. I propose therefore that the synthesis of appropriate enzymes related to digestion (of plant and animal tissue) as well as the synthesis of specific immune antibodies in relation to immunity reflect the expression of "lower" genome segments. This concept also has a special application in regard to the neurophysiology of auto-immunity and allergic reactions.

The Universal Human Genome and Immunity

Tissue recognized as “self” by the immune system does not elicit an immune response. Tissue or organisms perceived as foreign, will elicit an immune response (in the presence of an uncompromised immune system). Suppressed (methylated) segments of the universal genome coding for potentially foreign tissue or organisms do not elicit an immune response as long as they do not gain expression. In the event that a foreign-coding genome segment gains expression through demethylation, an immune reaction will inevitably occur. Allergic or auto-immune activity may then be explained on the basis that primitive genome segments similar to the challenging antigen may be expressed due to partial desuppression. The specific immune response would then be directed both at the invading organism as well as at the cells expressing the similar antigen. As regards an immune reaction following the exposure to foreign material or chemical, demethylation and expression of a potentially foreign coding genome segment may occur. The desuppressed and expressed primitive genome then stimulates an immune reaction. These situations would elicit an appropriate immune response to foreign, “non-self” tissue expression. More recent research has demonstrated the existence of viral DNA incorporated within our genome. It would appear that the exposure of this specific viral segment, referred to as endogenous viruses (erv’s) may initiate the specific immunological response. Studies have indeed shown that on removal of the erv’s through CRISPR CAS 9, the immune response was markedly impaired.

Current thinking regarding the generation of appropriate antibodies to a given antigen/pathogen is based on a process of high intensity mutations at the genome level so as to emerge with the appropriate antibody ‘fit’ (somatic hypermutation). I differ with this theory and contend rather that the fundamental core genome for the manufacture of the appropriate antibody is based on the existence of the erv’s.

The inflammatory reaction is the vital first phase of the immune response. Inflammation is initiated by the activation of inactive cytoplasmic NF-Kb by pro-inflammatory cytokines as well as by raised adrenaline levels. This together with activated STAT’S upregulates the appropriate segment of the genome to produce further pro-inflammatory cytokines and thus the inflammatory component is perpetuated. It should be noted for completeness that raised adrenaline and pro-inflammatory cytokines may also reflect the mind states of fear-anxiety-anger as well as degrees of hopeless-helplessness respectively.

Activated NF-kB additionally suppresses P53 in the cytoplasm. P53 is responsible for correcting abnormal progeny DNA splicing and will implement

apoptosis if the progeny genome remains compromised. In this way, chronic inflammation may further give rise to neoplasia based on its suppression of P53.

Thus it is proposed that inflammation, allergic reactions, auto-immunity and neoplasia represent a continuum of pathological conditions in which segments of the genome, coding for potentially foreign organisms or tissue, are expressed and elicit an immune response in the case of allergic reactions and auto-immunity. The initiating factors appear to be inflammation and the pathogen/allergen which 'bares' or desuppresses the appropriate genome segment. This may lead to allergy/autoimmunity. Genetic factors appear to play a part in maintaining the 'bared' or desuppressed genome segment. Environmental factors may also play a part in that exposure to pathogen/allergen may be absent at the critical time of immune maturity. Alternatively exposure to an allergen simultaneously with an episode of inflammation could possibly contribute to a similar outcome. Finally, completing the possibilities of chronic inflammation, neoplasia may result from the prolonged suppression of P53.