Identification of the gene encoding Brain Cell Membrane Protein 1 (BCMP1), a putative four-transmembrane protein distantly related to the Peripheral Myelin Protein 22 / Epithelial Membrane Proteins and the Claudins

ABSTRACT

A gene encoding a putative four-transmembrane protein, BCMP1, has been detected in multiple mammalian species, which is regarded as supplementary information within this family. The gene is abundant in dog brain cells and is believed to cause X-linked mental retardation due to its chromosomal localization in humans.

INTRODUCTION

Gene function is often studied in Background Model organisms (like the fruit fly Drosophila melanogaster and the nematode Caenorhabditis elegans) where genes with similar sequences can be identified within the human genome, allowing extrapolation from Drosephala and/or C. escherim and possibly from these two extant species to predict human gene function. Extrapolation relies on orthologous genes that originate from the same ancestral gene in the common ancestor of the model organism and humans. Correct identification of such relationships is crucial for optimal extrapolating function. Typically, these identifications are conducted through database comparisons with algorithms like BLAST, where the sequences that score the highest are assumed to be orthologs. Further criteria can be used to confirm the orthologous relationships, such as ensuring that orthologues share similar domain structures and confirming that no sequence from a distant taxon is more closely related to one proposed orthoLOG than to another. In addition, molecular phylogenetic reconstruction of gene family history may be employed in more complex analyses. Reconstructions enable the differentiation of speciation from gene duplication, thereby indicating orthologous and paralogously related relationships. With the near-completement of the human, C. elegans and Drosophila genomes, it is becoming possible to apply these relationships to analyses of large, complex gene superfamilies in the Metazoa. Reconstructing the minimum gene complement of a particular superfamily that would have been present in the last common ancestor of all three taxa is done through this process, which also provides information about the complexity of the bilaterian common-ancestors due to their phylogenetic relationship. The C2H2 ZNF superfamily, which has over 600 members in humans, accounts for 1-2% of all human genes and is the focus of our analysis. The C2H2 ZNF genes mainly encode DNA- and chromatin-binding transcription factors, and their repertoire comprises familiar and extensively researched developmental genes like Krox-20, snail, Gli, Krüppel, or hunchback, as well as several other genes with unknown function. We plan to reconstruct the minimum complement of C2H2 ZNFs present in the bilaterian common ancestor by defining orthologous relationships within this superfamily.

CONCLUSION

According to the new findings, clonal expansion is a prevalent feature in the B-cell repertoire of patients with rheumatoid arthritis. This expansion involves resting memory B cells and activated B cell repertoires, some of which are derived from the memory Brain tumor's internal compartment. As the range of clonal expansions increases, from the bloodstream to the synovial compartment, the narrowing of diversity indicates that these

antigens located in the brain are responsible for these "antigen-receptor biases," and evidence suggests that some of these expansion patterns may be joint-specific. Due to the rarity of identical clones in two distinct joints, immune reactions are likely unique to each joint. Additionally, B cells from this joint are unlikely to contain a different foreign antigen, so they are reacting with autoantigens produced locally, potentially by local tissue breakdown. Lymphoid aggregates that contain the cellular components of an ectopic germinal center can be formed in synovial tissue of rheumatoidic arthritis patients, as new research has shown, and can maintain B-cell clonal expansion and diversification. It is likely that the B cells that mature in these 'pseudogerminal centers' and those that we have identified in the current studies are responding to specific (auto)antigens. Hence, the identification of antigenic reactivations of these B cells, and specifically of those within the memory compartment that have probably "passed over (auto)antigen and T cell selection and rescue"; in this case, they may provide important clues about the role of B lymphocytes and their immunoglobulin molecules in the immunopathogenesis of rheumatoid arthritis.