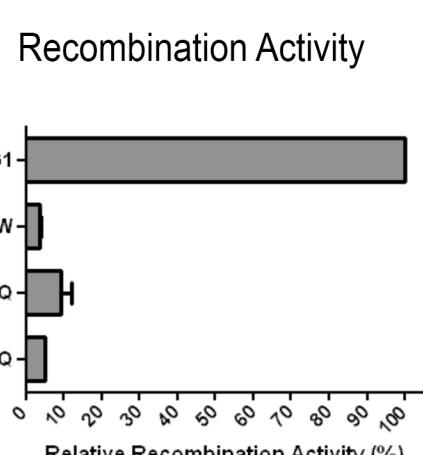
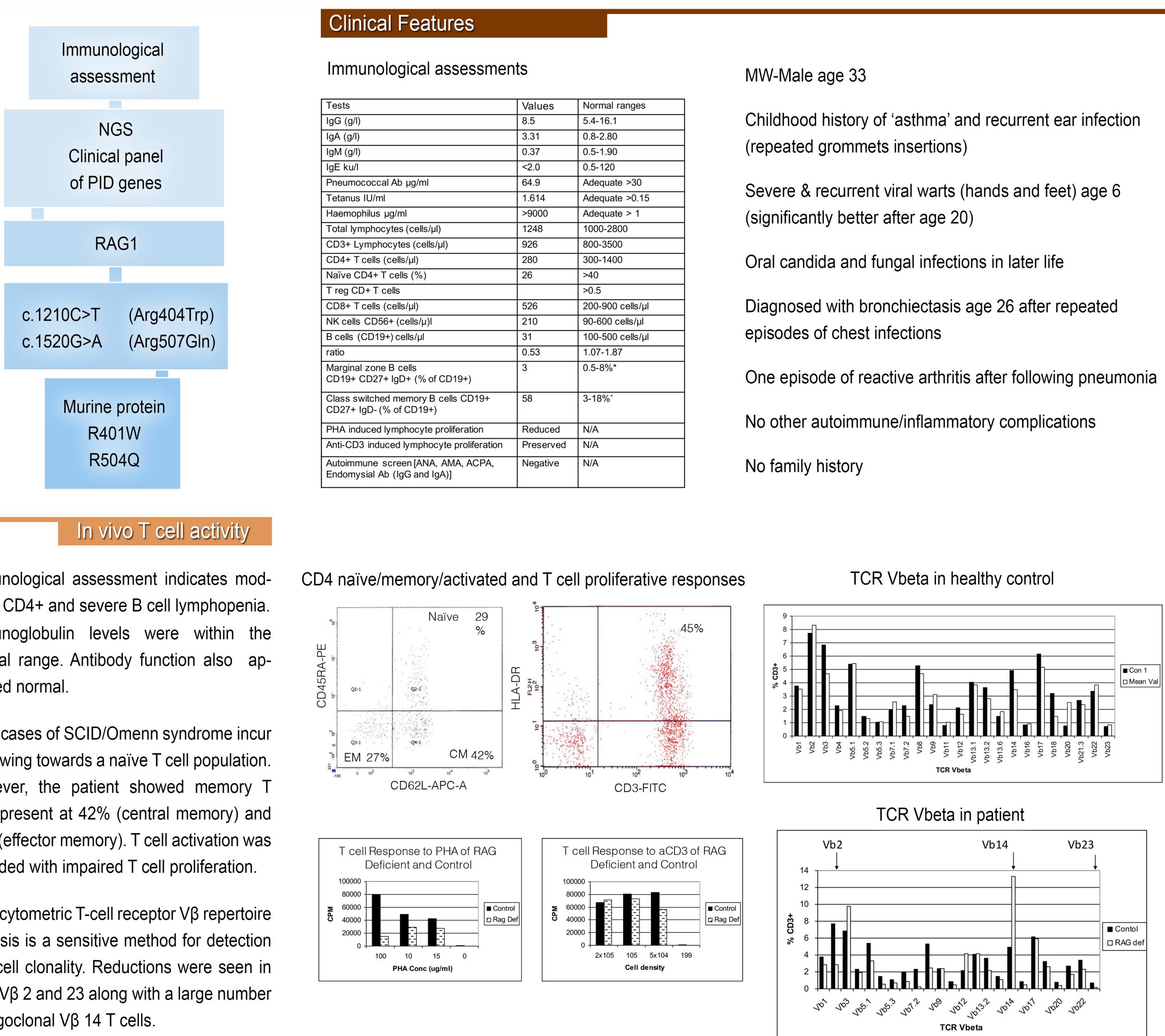


A novel case of RAG1 (Recombination Activating Gene) deficiency presenting with immunodeficiency in adulthood

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Mutations in the recombination activating genes (RAG) have been reported to cause severe combined immunodeficiency (SCID). Hypomorphic mutations may result in oligoclonal T cells responsible for an Omenn syndrome phenotype. RAG1 mutations resulting in immunodeficiency generally present at an early age. The increased use of whole exome and whole genome sequencing methods has resulted in deeper investigation of primary immunodeficiencies (PID). An increasing number of adult PIDs are now being identified. We present a case of biallelic missense mutations in RAG1 presenting with immunodeficiency in adulthood.



To assess the effect of mutation on protein function murine RAG1 constructs were produced. An extrachromosomal recombination assay was used based on RAG protein recognition of 12 and 23 nucleotide recombination signal sequences (RSSs) during V(D)J recombination. Both variants show loss of function.

With the increase of high accuracy NGS methods the identification of genetic determinants is becoming more frequent for adult PID. It is possible to investigate subtle protein functions through discovery of diseases with atypical presentation.

We report a case of biallelic mutations in RAG1 resulting in adequate immunoglobulin production and altered T cell activity. Identification of such cases are expected more frequently in the future.

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