process is known as a method of synthesizing homogeneous $Nd_2Fe_{14}B$ single phase powders [2]. In the HDDR process, $Nd_2Fe_{14}B$ grains disproportionate into a mixture of α-Fe, NdH_2 and Fe_2B by hydrogenation under high temperature hydrogen atmosphere. The subsequent desorption of hydrogen results in the recombination of the $Nd_2Fe_{14}B$ sub-micron grains. On the other hand, nano-structurization and hydrogenation of the Nd-Fe-B alloys by reactive mechanical milling have been successfully performed [3, 4], therefore, the synthesis of the nano-structure is expected to be fulfilled by the reactive mechanical milling [5]. In this work, we aim to synthesize Nd-Fe-B nanocomposite structure by the reactive mechanical milling process in a nanocomposite composition.

As a result of reactive mechanical milling, the $Nd_2Fe_{14}B$ grains result in a mixture of α-Fe, NdH_2 and amorphous, and the FWHM of the α-Fe and NdH_2 peaks were found to be in inverse proportional to the milling time. The change of the FWHM suggests that grains were refined by reactive mechanical milling. For this reason, it is expected that a nano-structure Nd-Fe-B powders will be obtained after recombination of the α-Fe and NdH_2 grains by a subsequent heat treatment. Detailed relationships among the microstructure, mechanical milling conditions, heat treatments and magnetic properties of the nanocomposites will be discussed at the symposium.

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Structural Biology of TIM proteins: A family of cell surface phosphatidylserine receptors that regulate immunity

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The T-cell immunoglobulin and mucin domain (TIM) proteins are involved in the regulation of immune responses by modulating effector Th1 and Th2 cell functions. The TIM gene family is located in a genomic locus linked to autoimmune disease and asthma both in mouse and humans and it has been associated with immune-related diseases, cancer and viral infections. The TIM are type I membrane proteins with an N-terminal immunoglobulin (Ig) domain followed by a heavily glycosylated mucin domain in the extracellular region, a single transmembrane region and a cytoplasmic tail with tyrosine phosphorylation motifs except in TIM-4. Whereas sequence identity among the Ig domains is high (40-60%), there are large differences in the length of the mucin domains. The N-terminal Ig domain is engaged in ligand binding with some contribution of the mucin domain. The structures of the Ig domains determined by our group provided relevant insights on ligand recognition by the TIM proteins. A loop disulphide linked to the CFG β-sheet of the Ig domain is a distinctive structural feature of the TIM proteins (1). Moreover, the structures identified a unique ligand-binding pocket with a metal ion to which ligands coordinate (Metal Ion-dependent Ligand Binding Site, MILIBS) (2). The TIM proteins use the MILIBS to bind to phosphatidylserine (PtdSer) and to mediate phagocytosis of apoptotic cells (2-4). A model for TIM protein binding to PtdSer in cellular membranes was built based on structural and functional data (3). In this model the tip of the N-terminal Ig domain of the protein penetrated into the membrane, whereas the hydrophilic moiety of PtdSer entered into the MILIBS. Moreover, we have seen that the MILIBS modulate the biology of the TIM proteins, such as the trafficking of TIM-1 to the cell surface, TIM-TIM interactions and the conformation of the proteins on the cell surface. Therefore, the MILIBS is a critical determinant of the ligand binding specificity and functional properties of the TIM family, such as the recognition of PtdSer on the surface of apoptotic cells. Overall, we conclude that the unique structure of TIM IgV domains suggests that the TIM molecules evolved as a family of pattern recognition receptors for PtdSer that determine whether apoptotic cell recognition leads to immune activation or tolerance, depending on the TIM molecule engaged and the cell type it is expressed on (5).

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Substrate recognition by complement convertases revealed in the C5-CVF complex

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The activation of complement triggers cleavage of the proteins C3 and C5 by proteolytic enzymes, the convertases. These contain a non-catalytic substrate contacting subunit (C3b or C4b) in complex with a protease subunit (Bb or C2a). We determined the crystal structures of the C3b homologue Cobra Venom Factor (CVF, 160 kDa) in complex with the 190 kDa protein C5, and in complex with C5 and the 23 kDa S. aureus inhibitor SSL7 at 4.3 Å resolution [1]. The structures reveal a parallel two-point attachment between C5 and CVF, where the presence of SSL7 only slightly affects the C5-CVF interface explaining the IgA-dependence for SSL7 mediated inhibition of C5 cleavage. CVF functions as a relatively rigid binding scaffold inducing a conformational change in C5 which positions its cleavage site in proximity to the serine protease Bb. A general model for substrate recognition by the convertases is presented based on the C5-CVF and the C3b-Bb-SCIN structures [2]. Prior knowledge concerning interactions between the endogenous convertases and their substrates is rationalized by this model.

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