TRIM21: A novel mammalian IgG-receptor that mediates autoimmune disease

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The newly identified human tripartite motif (TRIM) family comprise ~70 proteins that mediate innate immunity and other critical cellular functions(1). Despite their importance, very little is known about their molecular, kinetic and thermodynamic basis of function. Our work has revealed that the autoantigen TRIM21, which mediates Systemic Lupus Erythematosus, is a novel IgG receptor that is highly conserved across mammalian species. Our data show that TRIM21 is structurally and mechanistically unrelated to all previously identified IgG receptors and engages the Fc using a domain from a new protein superfamily - PRYSPRY - which our crystal structures define(2). The PRYSPRY domain determines TRIM function and our data establishes a common mechanism that is predictive of disease-causing polymorphisms in anti-HIV TRIM5α(3), TRIM18(4) and FMF-associated TRIM20/pyrin(5).

References

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