The role of Abl family kinases in autoimmune arthritis

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Background: The non-receptor tyrosine kinase c-Abl plays a role in various cell processes. It has an oncogenic counterpart, the Bcr-Abl fusion protein which causes certain human leukemias. Previous studies suggested, that the Abl tyrosine kinases play a role in the functions of mature myeloid cells. In this present study, we examined the function of Abl and its redundant protein Arg (Abl related gene) in a myeloid cell mediated autoimmune arthritis.
Materials and methods: The abl null mutation results in perinatal lethality, therefore to attain conditional deletion of Abl, mice carrying an Abl allele with flanked loxP sites(Abl^{flox}) were crossed with mice expressing the Cre recombinase from the myeloid-specific lysosyme M promoter ($LysM^{cre}$). By this crossing we generated $LysM^{cre/cre}Abl^{flox/flox}$ ($Abl^{\Delta myeloid}$) mice with Abl deficiency in the myeloid compartment. We also tested Arg-deficient ($Arg^{-/-}$) mice and Abl and Arg dual deficiency. Development of autoantibody-induced arthritis was induced using the K/BxN serum. The expression of Abl and Arg protein in various myeloid compartments (neutrophils, macrophages) was tested by immunoblotting.
Results: The genetic mutations ($Abl^{\Delta myeloid}$ and $Arg^{-/-}$) dramatically decreased the expression levels of these kinases in myeloid cells (neutrophils and macrophages). Both $Abl^{\Delta myeloid}$ and the Arg-deficient mice showed the same macroscopic signs of autoantibody-induced arthritis and the same arthritis-induced loss of articular function compared to wild type mice. In addition, the double mutation ($Abl^{\Delta myeloid}Arg^{-/-}$) also did not affect the diseases course.
Conclusions: Our results indicate that the Abl family kinases in myeloid cells (e.g. neutrophils) are not indispensable for the development of autoantibody-induced arthritis in experimental mice.

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