Background: Dendritic cells (DCs) play important roles in inducing immune response as well as maintaining immune tolerance. Src homology 2 domain-containing protein tyrosine phosphatase-1 (Shp1) is a negative regulator of signaling in hematopoietic cells and is expressed in a variety of immune cells including DCs. Shp1 homozygous mutant mice (motheaten mice) develop multiple immunological abnormalities and they die around four weeks after birth because of severe pneumonia. Motheaten mice produce large amounts of autoantibodies, and besides, B-1a cells, a distinct B cell subset, which are important source of autoantibodies increase in these mice. The functional abnormality of DCs in motheaten mice has not been characterized, but DCs and macrophages increase in various organs of motheaten mice.

To analyze the function of Shp1 in DCs, we generated Shp1 conditional knockout mice. The genotype of Shp1 in which Shp1 gene is specifically depleted in CD11c+ cells. We found that aged shp1-/- mice developed autoimmune glomerulonephritis. We also found that they developed severe tubulointerstitial nephritis (TIN) at the age of 40 weeks, which is characterized by the infiltration of CD11c+ and F4/80+ cells. CD4+ T cells from Shp1 KO mice produce much more amount of IFNγ. Collectively, Shp1 in DCs acts as a key regulatory molecule to protect against autoimmunity.

Objectives: We analyzed salivary glands of KO to confirm whether they have autoimmune salaiadentis because TIN is known to be the most obvious renal manifestations of Sjögren’s syndrome in human.

Methods: Shp1 KO are generated by crossing a mouse line carrying floxed Shp1 allele to mice expressing Cre recombinase under the control of the CD11c promoter. Sex- and age-matched Ptpn6<sup>−/−</sup> littermates without Cre gene were studied as controls. We analyzed secretory function of the salivary glands in response to pilocarpine stimulation in Shp1 KO at the age of 40 weeks or older. We then performed histological examination of salivary glands (submandibular glands and sublingual glands) with light-microscopy and immunohistochemical staining. The mononuclear cells prepared from the salivary glands were analyzed by flow cytometry (FCM). We also quantified anti-SSA/Ro60 antibodies and anti-SSB/LA antibodies by ELISA.

Results: Shp1 KO secreted less saliva flow compared to control mice by pilocarpine stimulation. Histological study showed Shp1 KO exhibited massive infiltration of inflammatory cells in salivary glands associated with perifocal and periductal fibrosis. Most of infiltrated cells were stained by anti-CD3 or B220 nAbs. FCM revealed that B cells increased in the salivary glands of Shp1 KO. In addition, B-1a cells also increased in the salivary glands of the mice. The levels of anti-SSA/Ro60 antibodies and anti-SSB/LA antibodies were increased in Shp1 KO.

Conclusion: CD11c-specific ablation of Shp1 induces the ectopic generation of lymphoid structure in salivary glands and impairment of salivary secretion. Autoantibody profile in Shp1 KO resembled that in human Sjögren’s syndrome. Our findings suggest that aged Shp1 KO have the potential to become a new mouse model for the analysis of Sjögren’s syndrome.

References:

Disclosure of Interests: Masato Kinoshita: None declared, Yoriaki Kaneko Grant/research support from: CHUGAI PHARMACEUTICAL CO., LTD. Astellas Pharma Inc. b. Speakers bureau: CHUGAI PHARMACEUTICAL CO., LTD. Astellas Pharma Inc., Mitsubishi Watanabe: None declared, Yoichi Imai: None declared, Shreya Shrestha: None declared, Junya Suwa: None declared, Yuko Oishi: None declared, Hiroko Hamatani: None declared, Masao Nakasatomi: None declared, Toru Sakairi: None declared, Hidekazu Ikeuchi Speakers bureau: CHUGAI PHARMACEUTICAL CO., LTD.


DOI: 10.1136/annrheumdis-2020-eular.1044
Objectives: The relationship between pregnancy and arthritis is a complex one. Because of the variability of arthritic conditions, it is important for patients to get advice from their doctor or a specialist nurse before trying for a baby. There can be implications for medication regimes, while the pregnancy itself can also affect the inflammatory arthritis. In the postpartum period, other considerations include breastfeeding and the frequent return of flares. Through this education programme, Arthritis Ireland developed information resources primarily targeting women of child-bearing age. The multichannel campaign provided information about the wide range of issues of concern to women with inflammatory arthritis who are planning a family or are pregnant.

Objectives:
• To provide information and increase awareness around inflammatory arthritis and pregnancy;
• To support women living with inflammatory arthritis through their illness and life journey;
• To increase awareness of the work of Arthritis Ireland as a patient organisation.

Methods: A multi-channel approach was taken to the development, production and dissemination of information, with public information events, literature and a suite of videos developed. Up to this point, there had not been any Irish-produced material on this subject. The topic was seen to be an important one and an issue of significant public health interest. The series of information talks on pregnancy and inflammatory arthritis was delivered by consultant rheumatologists and were held in cities around Ireland. The information booklet covered topics such as planning for a baby, medication and pregnancy, the role of the father, fertility, genetics, during the pregnancy, the impact of the disease on fertility, and the role of the father. In the postpartum period, other considerations include breastfeeding and the frequent return of flares.

Video was seen to be central to the success of the campaign. Working with the expert healthcare team, six information videos were developed around obstetrics, rheumatology, physiotherapy and occupational therapy. The videos were published and promoted across Arthritis Ireland’s social media channels and within the expert healthcare team. The capstone video featured a young mother who was diagnosed with JIA when she was two. Her story was an incredibly powerful testimony of overcoming and dealing with adversity and complex health issues. The capstone video featured a young mother who was diagnosed with JIA when she was two. Her story was an incredibly powerful testimony of overcoming and dealing with adversity and complex health issues.

Results: This educational campaign was developed to meet a significant need in the health information landscape. While there are no local resources produced focusing on pregnancy and parenting, there wasn’t anything in Ireland which specifically addressed the needs of women and men with inflammatory arthritis who are looking to have a family. The materials produced are a valuable asset for Arthritis Ireland’s campaign of patient education materials.

Conclusion: It is anticipated that the materials developed will have a long lifespan and will support prospective parents for several years to come. Central to the success of the project was the involvement of the expert healthcare teams. Their commitment to the project spoke volumes of its importance and the considerable need for the clearly communicated information, which the project provided.