

[Close Window](#)

ATS 2008 · Toronto International Conference

Abstract Number: 2077

Contact/Presenting Author: Hiroe Sato

Department/Institution: Clinical Genomic Group, Royal Brompton and NHLI, Imperial College

Address: EKB, 1B Manresa Road

City/State/Zip/Country: London, SW3 6LR, England

Phone: 44-20-7351-8354 **Fax:** 44-20-7351-8336 **E-mail:** h.sato@imperial.ac.uk

ATS member: No **Student or in training:** No

Abstract Category: 09.39 - All - Sarcoidosis: Mechanisms

Presentation format: Either Poster or Oral

Travel Award: No

Publication of email address: No

I confirm that all authors listed on this abstract have knowledge of the abstract submission:
Yes

Title: Caspase Recruitment Domain (CARD) 15 Polymorphisms Are Associated with Severe Pulmonary Sarcoidosis

H.. Sato, M.D., Ph.D.¹, H..R.T.. Williams, M.D.^{1,2}, P.. Spagnolo, M.D.¹, A.. Abdallah, Ph.D.¹, T.. Ahmad, M.D., Ph.D.³, T..R.. Orchard, M.D.², S..J.. Copley, M.D.⁴, S..R.. Desai, M.D.⁵, A..U.. Wells, M.D.¹, R..M.. du Bois, M.D.¹ and K..I.. Welsh, Ph.D.¹. ¹Clinical Genomics, Royal Brompton Hospital & NHLI, Imperial College, London, England; ²Department of Gastroenterology, Imperial College, London, England; ³Gastroenterology Unit, University of Oxford, Oxford, England; ⁴Radiology Department, Hammersmith Hospital, London, England and ⁵Department of Radiology, King's College Hospital, London, England.

Introduction: Sarcoidosis and Crohn's disease (CD) are heterogeneous systemic diseases characterised by granulomatous inflammation. CARD15 is a major susceptibility gene for ileal and fibrostenotic CD. The CCR5 gene is associated with both severe pulmonary sarcoidosis and perianal CD. We hypothesised that CARD 15 polymorphisms would be associated with severe pulmonary sarcoidosis. We also stratified by CCR5 genotype.

Methods: 185 UK sarcoidosis patients and 354 UK healthy controls were genotyped for 5 CARD15 snps. We investigated the carriage of the CCR5 HHC haplotype in these sarcoidosis patients. Pulmonary function tests and chest X-ray at presentation and follow ups were examined for associations with the genetic data.

Results: CARD15 genotypes did not differ between sarcoidosis patients and controls. However, sarcoid patients carrying the functional R702W CARD15 snps were more likely to have lung

fibrosis at 4 years' follow up ($p < 0.05$). All patients possessing both R702W and CCR5 HHC haplotype had lung fibrosis at presentation. Carriage of R702W was associated with worse FEV₁ at presentation ($p < 0.05$), 2 years ($p < 0.05$), and 4 years ($p = 0.05$), while carriage of the CARD15 1761G allele was associated with better lung function ($p = 0.02$ for FEV₁, $p = 0.01$ for FVC, and $p = 0.001$ for TLCO at presentation); a significant gene-dose effect was observed.

Conclusion: For the first time, an association between two CARD15 polymorphisms and specific sarcoidosis phenotypes has been demonstrated, as well as an additive effect of possessing the CARD15 R702W, CCR5 HHC haplotype.

Funded By: Asmarley Trust.

FACULTY DECLARATION OF INTEREST:

1. PERSONAL FINANCIAL INTERESTS:

As the presenting author of this abstract, please check the YES box if you have had a financial relationship with a commercial entity within the past 12 months in relation to this abstract or expect to have such a relationship in the time prior to or during the 2008 International Conference. If you did not have a financial relationship with a commercial entity in the past 12 months and do not expect to have a relationship prior to the 2008 Conference, check the NO box and proceed to the next question. Please note: Known Personal financial interests of spouses or life partners should also be noted.

Financial Disclosure: No

2. PUBLIC STATEMENTS OR POSITIONS:

Please check the YES box below if you have made any public statements relevant to this abstract that could affect your objectivity or independence in the session or the perception of others to your objectivity or independence. A public statement includes, but is not limited to an editorial, a statement made to a news network, a statement made during testimony, etc. Please also describe the statement made and the commercial entity affiliated with the statement, if any. If you have not made any public statement, check the NO box. **No**

Public Statement or Position	Commercial Entity (if applicable)
-------------------------------------	------------------------------------------

3. INSTITUTIONAL FINANCIAL INTERESTS:

Are you are aware of any financial relationship your institution or employer may have with a commercial entity in relation to this abstract and provide the name of the commercial entity. Please note: in regard to this issue, the ATS does not require individuals to make specific inquiries of the authorities of their institution. **No**

Institution	Financial Relationship	Commercial Entity
--------------------	-------------------------------	--------------------------

4. TOBACCO INDUSTRY INTERESTS:

Please check the YES box below if within the past ten years you have had a professional relationship with, or personal financial interests (other than mutual funds) in, any of the following: (1) a company engaged in the manufacture of tobacco products; (2) an affiliate or subsidiary of

such a company for which there is reasonable indication that the affiliate or subsidiary's ownership, activities, and/or image benefits the sale of tobacco products; (3) an advocacy group known to have received tobacco industry support to promote the use of tobacco products and/or impede policies to prevent tobacco-caused disease. Known relationships of spouses or life partners with the tobacco industry should also be noted. Please indicate the time of each relationship by checking the appropriate box below. If you do not have a tobacco industry relationship, check the NO box. (Note: This disclosure is for information only and will not affect the eligibility of ATS-2008 faculty.) **No**

Relationship	Tobacco Entity	Time of Relationship
--------------	----------------	----------------------

5. OFF-LABEL DISCUSSION:

Disclosure of any discussion in the presentation of **“off-label” (unapproved) use of substances/products** not approved in the United States for the use under discussion. (U.S. Food and Drug Administration Guidance for Industry: Industry-Supported Scientific and Educational Activities). Please check the YES box below if your presentation of this abstract will include discussion of **“off-label” (unapproved)** use of a commercial product or an investigational use not yet approved in the United States for the use under discussion and provide specific information in the box below. If you will not be discussing any off-label product use, check the NO box. **No**

6. OTHER:

If there is anything else that could affect your objectivity or independence or the perception by others of your objectivity and independence in relation to this abstract, please briefly.

I hereby confirm the Disclosure information above is accurate at the time of this submission. I acknowledge that keying in my name and date of completion below indicates assent to this agreement and is equivalent to my signature.

Presenter First Name: Hiroe
Presenter Last Name: Sato
Date: 31st Oct 2007