Silica induces pulmonary fibrosis and also autoimmune diseases

- Silicosis
- Systemic sclerosis
- Rheumatoid arthritis (Caplan’s syndrome)
- SLE
- ANCA-related vasculitis/nephritis

Silica may activate responder T cell and also regulatory T cell

- CD4+CD25+FoxP3+ regulatory T cell
- Excessive loss of Treg

Functional analysis of peripheral CD4+25+ fraction from healthy donors and silicosis

Silica gradually activates peripheral responder T cell

Expression of PD-1 (Activation marker of T cell) in peripheral CD4+25+ or 25- fraction from healthy donor and silicosis

Regulatory T cells from silicosis are highly sensitive to the CD95-mediated apoptosis than those from health donors

Activated responder T cells due to co-culture with silica enter CD4+25+ fraction

in vitro silica exposure to PBMC causes loss of FoxP3+ regulatory T cells
In vitro silica exposure to PBMC causes loss of FoxP3+ regulatory T cells–time course–

**FACS analysis**

Healthy Donors

PBMC

Silica 25–50 μg/ml

PBMC: 1×10^6/ml

24 h at bottom

CD25+ including activated T cells

- **Silica activates both responder and regulatory T cells**
- **Causes loss of Treg and reduced regulatory function**

### Silica activates both responder and regulatory T cells and causes loss of Treg and reduced regulatory function

**CD4+CD25+Foxp3+**

Silica

CD4+CD25+T responder

CD25

CD95 (Fas)

CD95-mediated apoptosis

Excessive loss of Treg

Reduced number and function of Treg

Activation of Autoimmunity

### Silicosis patients including higher activated T cells in their peripheral blood

**CD4+CD25+**

Silica

Percentage (%)

Day 1 vs. Day 4

### Acknowledgements

- **Department of Hygiene, Kawasaki Medical School**
- **Present Staff**
  - Prof. Susumu Nakamura
  - Dr. Yoshihito Hamada
  - Dr. Naoko Ueki
  - Ms. Shoko Yamamoto
  - Ms. Naomi Miyahara

- **Former Staff**
  - Prof. Akihito Uchida
  - Dr. Hiroyuki Hayashi
  - Ms. Shoko Yamamoto
  - Dr. Ying Chen
  - Dr. Hiroaki Hayashi
  - Dr. Megumi Maeda

"Comprehensive approach on asbestos-related diseases" supported by the "Special Coordination Funds for Promoting Science and Technology (H18), 2006 to 2010 in Japan"

Chief: Prof. Takashi Nakano; Respiratory Medicine, Department of Internal Medicine, Hyogo College of Medicine

Associate Chief: Prof. Takemi Sakaguchi, Department of Molecular Oncology, Aichi Cancer Center Research Institute

Dr. Hiroshi Nishimoto; Department of Pathology and Biological Responses, Graduate School of Medicine, Hiroshima University

Dr. Hideaki Nishimoto; Department of Respiratory Medicine, Department of Internal Medicine, Hiroshima University

Prof. Shinya Nishimoto; Department of Respiratory Surgery, Research Institution for Radiation Biology and Medicine, Hiroshima University

Prof. Kazuya Fukuoka; Department of Surgery, Okayama University School of Medicine

Ms. Yoko Kojima; Department of Respiratory Surgery, Department of Internal Medicine, Hyogo College of Medicine

Ms. Hinako Sakaguchi; Department of Respiratory Surgery, Research Institution for Radiation Biology and Medicine, Hiroshima University

Ms. Suna Tanayo Hatayama; Department of Radiology, Hyogo College of Medicine

Ms. Minako Umeki; Department of Pathology, Hyogo College of Medicine

Ms. Naoko Usui; Department of Radiology, Hyogo College of Medicine

Ms. Yoko Kojima; Department of Respiratory Surgery, Department of Internal Medicine, Hyogo College of Medicine

Associate Chief: Prof. Takashi Nakano; Respiratory Medicine, Department of Internal Medicine, Hyogo College of Medicine

Associate Chief: Prof. Takemi Sakaguchi, Department of Molecular Oncology, Aichi Cancer Center Research Institute