Biological effects of low level exposure to trichloroethylene (TCE): Recent findings from the National Cancer Institute

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# **Principal Investigators**

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## Rationale

 To study early biologic effects of TCE at airborne exposure levels below the U.S. occupational standard, 100 ppm as an 8-hour time weighted average.

 To provide insight into carcinogenic mechanism of TCE exposure, especially for non-Hodgkin lymphoma and kidney cancer.

#### **Molecular Epidemiology Study of TCE**

Study design:

- <u>40</u> factories in Guangdong, China were screened to identify factories that used TCE with <u>none to minimal</u> use of other chlorinated solvents
- <u>6</u> metal cleaning factories selected: 80 workers exposed almost exclusively to TCE were enrolled
- 96 unexposed controls were enrolled from 2 clothes and 1 food factory
- Extensive personal air monitoring for TCE
- Blood and urine samples collected





#### Leucocyte (white blood cells) Subsets

- Myeloid lineage
  - » Granulocytes
  - **»** Platelets
  - » Monocytes
- Lymphoid lineage
  - » T-cell subsets
  - » B cells
  - » NK cells

#### TCE Exposure and Peripheral Blood Cell Counts and Lymphocyte Subsets



Lan et al., Carcinogenesis 2010 Hosgood...Lan, Front Oncol 2012

#### p values are for trend

#### **Cytokines and Antibodies in Peripheral Blood Serum**

- Cytokines are cell signaling molecules that aid cell to cell communication in immune responses:
  - -sCD27
  - sCD30
  - IL-10
- Antibodies:
  - IgG
  - -igM

# **TCE Exposure and Immunologic Markers**

\*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001; \*\*\*\*: p<0.0001



Lan et al., Carcinogenesis 2010; Bassig...Lan, Environ Mol Mutagen 2013; Zhang...Lan, Carcinogenesis 2013

# **Conclusions and Implications of TCE Study**

- TCE exposure → alterations in multiple immune markers
- Supports biological plausibility that TCE may cause NHL
- All effects occurred at exposures < 12 ppm, raising a concern about the current US OSHA standard of 100 ppm

# Impact of Research Findings

#### IARC Monograph (Volume 106, 2012) – Group I

TCE causes kidney cancer, and possibly NHL

#### EPA risk assessment of TCE exposure (2014)

• TCE is carcinogenic to humans

- Lan et al. (2010) Occupational exposure to trichloroethylene is associated with a decline in lymphocyte subsets and soluble CD27 and CD30 markers. Carcinogenesis 31:1592-6.
- Hosgood et al. (2012) Decreased numbers of CD4+ naïve and effector memory T cells, and CD8+ naïve T cells, are associated with trichloroethylene exposure. Frontiers in Oncology 1:1-6.
- Vermeulen et al. (2012) Elevated urinary levels of kidney injury molecule-1 among Chinese factory workers exposed to trichloroethylene. Carcinogenesis 33: 1538-41.
- Bassig et al. (2013) Occupational exposure to trichloroethylene and serum concentrations of IL-6, IL-10, and TNF-alpha. Environ Mol Mutagenesis 54: 450-4.
- Zhang et al. (2013) Alterations in serum immunoglobulin levels in workers occupationally exposed to trichloroethylene. Carcinogenesis 34: 799-802.