信州大学 ENCs ワークショップ講演会

「安全なナノ材料設計と標準化（Design Safe Nano & Standardization)」

開催日時：2013 年 10 月 25 日 13:00-15:30
開催場所：信州大学工学部（長野市）長野市ものづくり支援センター(UFO)5 階
主催　：信州大学エキゾチック・ナノカーボンの創成と応用プロジェクト拠点
議長　：信州大学特任教授　鶴岡秀志

[開催の辞]

既に多くの工業製品に活用されているナノテクノロジーですが、中でもナノカーボン材料の応用開発と工業化は益々重要となっています。他方、安全と社会受容を材料研究・技術開発と協調して進めることは、カーボンナノチューブ(CNT)の安全性評価を契機として国際的に当然のことと受け止められるようになってきました。本年 4 月に米国国立労働安全衛生研究所(NIOSH)が発表した CNT/CNF の安全情報 CIB 65 では MWCNT による呼吸器ばく露によるリスク予測確率の概念が強く示されています。また、個々の CNT の物性と安全性の関係を研究することの重要性も指摘しています。他方、今年前半より欧米各国は応用製品の環境安全性研究を含めた CNT の応用技術開発に注力する姿勢を鮮明にしています。

前述の国際的動向を鑑みて安全なナノ材料の設計を目指す視点を中心テーマとしてナノカーボンに関わる皆様の情報提供の場としてワークショップを開催致します。講師にはそれぞれ政府プロジェクトに密接に関わっているにもかかわらず、日本でほとんど講演をされていない Prof. Holian（モンタナ大学環境健康科学センター）, Dr. Nguyan（米国国立標準技術研究所（NIST)）, Prof. Vogal（デンマーク国立労働環境研究所（NRCWE)）にレクチャーしていただく事になりました。

ナノカーボンを中心とした Design Nano Safe の視点から見た最新の安全性評価及びナノ構造の姿、それを巡る規格化について活発な議論の場として皆様に参加していただきたく思います。

[講師と講演タイトル]

I. 開会の辞 [13:00-13:10]

信州大学特別特任教授 遠藤守信

II. 講演

1. Andrij Holian [13:10-13:50]

Professor, Director, Center for Environmental Health Science, University of Montana, USA.

演題：NLRP3 Inflammasome Activation in Nanoparticle-Induced Lung Inflammation

[Abstract]

Inhalation exposure to certain micron and nano-sized materials cause lung inflammation that can progress to lung fibrosis depending on dose and lung retention. Increasing evidence over the past few years provides support that alveolar macrophages are critical pulmonary immune cells that regulate the inflammatory response to particulates. Alveolar macrophages are innate immune cells in the lung responsible for clearance of inhaled materials, but also distinguish certain particulates as danger signals that can cause an inflammatory response. The inflammatory response is initiated when certain phagocytosed particulates cause phagolysosomal membrane permeability (LMP) releasing cathepsin B into the cytoplasm and activating NLRP3 inflammasome assembly, caspase-1 activation and cleavage of pro-IL-1β into its active form. Importantly, in vitro release of IL-1β correlate with in vivo inflammation and pathology. A critical step in this inflammatory process is LMP, but the exact mechanism is not yet understood. Asbestos fibers, crystalline silica and certain nanomaterials cause LMP and generation of reactive oxygen species has been proposed to contribute to LMP. Interestingly, AM uptake of crystalline silica and nano silver by the scavenger receptor MARCO increases uptake, but decreases IL-1β release and inflammation. Testing of various series of nanomaterials demonstrate that length and surface characteristics are important determinants of LMP. Increasing the aspect ratio and/or rigidity of nanomaterials increases bioactivity, while carboxylation of ENM surfaces decreases bioactivity. In

addition, certain metals, such as nickel, on carbon nanotubes increases LMP. Very good correlation in IL-1β release was observed among different macrophage models including THP-1 cells, primary macrophages from mice and human alveolar macrophages. Furthermore, the in vitro IL-1β release correlates very well with in vivo inflammation and pathology suggesting that THP-1 cells can be used for high throughput screening of various nanomaterials.

2. Ulla Vogel [13:55-14:30]
Professor, PI of Danish Center for Nanosafety, National Research Centre for the Working Environment

演題：Carbon Based Nanomaterials and Human Health-Safe Design

[Abstract]

Carbon-based nanomaterials constitute a large new group of nanomaterials with potential widespread use. There is now amble evidence that free, insoluble nanoparticles are generally more harmful to human health than the corresponding bulk chemicals, especially when airborne particles are inhaled.

We have focused our research on industrially relevant high volume materials including carbon black nanoparticles and carbon nanotubes. We assess toxicity using intratracheal instillation of nanomaterial and assess the toxicity using delineation of global gene expression in combination with biomarkers of inflammation and DNA damage.

Both carbon black and carbon nanotubes are efficient producers of reactive oxygen species (ROS)(1). Furthermore, we have shown that carbon black nanoparticles are mutagenic in vitro and that the mutation spectrum indicates that ROS are the likely cause of the mutations (2). Pulmonary exposure studies in mice suggest that pulmonary exposure to nanosized carbon black at current Danish occupational exposure limits (3.5 mg/m^3) causes DNA stand breaks and inflammation in lung and liver tissues (3-4). Similarly, pulmonary exposure to carbon nanotubes induce adverse effects at low exposure doses (5-7). On the other hand, the limited available literature

on embedded nanoparticles suggest that nanoparticle toxicity is reduced in dust from composite materials that contain nanoparticles (8-11).

The adverse outcomes that may be relevant in relation to inhalation of carbon nanoparticles include cancer (12), cardiovascular disease (13-14), fertility (15) and reprotoxic effects (16). The results suggest that exposure to airborne nanoparticles should be regulated especially in the working environment.

[Reference List]

1. Jacobsen, N. R., Pojana, G., White, P., Moller, P., Cohn, C. A., Korsholm, K. S., Vogel, U., Marcomini, A., Loft, S., and Wallin, H. (2008) *Environ. Mol. Mutagen.* **49,** 476-487
2. Jacobsen, N. R., White, P. A., Gingerich, J., Moller, P., Saber, A. T., Douglas, G. R., Vogel, U., and Wallin, H. (2011) *Environ. Mol. Mutagen.* **52,** 331-337
3. Bourdon, J. A., Saber, A. T., Jacobsen, N. R., Jensen, K. A., Madsen, A. M., Lamson, J. S., Wallin, H., Moller, P., Loft, S., Yauk, C. L., and Vogel, U. B. (2012) *Part Fibre Toxicol.* **9,** 5
4. Saber, A. T., Bornholdt, J., Dybdahl, M., Sharma, A. K., Loft, S., Vogel, U., and Wallin, H. (2005) *Arch Toxicol* **79,** 177-182
5. Ma-Hock, L., Treumann, S., Strauss, V., Brill, S., Luizi, F., Mertler, M., Wiench, K., Gamer, A. O., van, R. B., and Landsiedel, R. (2009) *Toxicol. Sci.* **112,** 468-481
6. Pauluhn, J. (2010) *Toxicological Sciences* **113,** 226-242
7. Kato, T., Totsuka, Y., Ishino, K., Matsumoto, Y., Tada, Y., Nakae, D., Goto, S., Masuda, S., Ogo, S., Kawanishi, M., Yagi, T., Matsuda, T., Watanabe, M., and Wakabayashi, K. (2013) *Nanotoxicology.* **7,** 452-461
8. Saber, A. T., Jacobsen, N. R., Mortensen, A., Szarek, J., Jackson, P., Madsen, A. M., Jensen, K. A., Koponen, I. K., Brunborg, G., Gutzkow, K. B., Vogel, U., and Wallin, H. (2012) *Part Fibre Toxicol.* **9,** 4
9. Saber, A. T., Koponen, I. K., Jensen, K. A., Jacobsen, N. R., Mikkelsen, L., Moller, P., Loft, S., Vogel, U., and Wallin, H. (2012) *Nanotoxicology.* **6,** 776-788
10. Saber, A. T., Jensen, K. A., Jacobsen, N. R., Birkedal, R., Mikkelsen, L., Moller, P., Loft, S., Wallin, H., and Vogel, U. (2012) *Nanotoxicology.* **6,** 453-471
11. Wohlleben, W., Brill, S., Meier, M. W., Mertler, M., Cox, G., Hirth, S., von, V. B., Strauss, V., Treumann, S., Wiench, K., Ma-Hock, L., and Landsiedel, R. (2011) *Small*
12. Takagi, A., Hirose, A., Futakuchi, M., Tsuda, H., and Kanno, J. (2012) *Cancer Sci.* **103,**

1440-1444

13. Halappanavar, S., Jackson, P., Williams, A., Jensen, K. A., Hougaard, K. S., Vogel, U., Yauk, C. L., and Wallin, H. (2011) *Environ Mol Mutagen* **52,** 425-439
14. Bourdon, J. A., Halappanavar, S., Saber, A. T., Jacobsen, N. R., Williams, A., Wallin, H., Vogel, U., and Yauk, C. L. (2012) *Toxicol. Sci.*
15. Kyjovska, Z. O., Boisen, A. M., Jackson, P., Wallin, H., Vogel, U., and Hougaard, K. S. (2013) *Reprod. Toxicol.* **36,** 88-97
16. Jackson, P., Hougaard, K. S., Vogel, U., Wu, D., Casavant, L., Williams, A., Wade, M., Yauk, C. L., Wallin, H., and Halappanavar, S. (2012) *Mutat. Res* **745,** 73-83

3. Tinh Nguyen [14:30 – 15:10]

Dr., Physical Scientists, Engineering Lab. National Institute of Standards and Technology, United States

演題：Mechanism of Nanomaterial Release by UV Irradiation of Polymer Nanocomposites

[Abstract]

Nanomterials, such as CNTs, metal oxides, are being incorporated in polymer matrices (i.e., polymer nanocomposites) to enhance multiple properties. These advanced composites are increasingly used in a variety of applications under harsh environments. Because polymers undergo degradation when exposing to weathering environments, nanomaterials in polymer nanocomposites may be released into the environments during the composites' life cycle. Such release potentially poses an environmental health and safety (EHS) problem and may hinder commercialization of these advanced materials. NIST has investigated the effects of MWCNTs, silica nanoparticles, and graphene oxides on the photodegradation of some important polymers and the mechanism of nanomaterial release from the nanocomposites irradiated with ultraviolet (UV) radiation. This talk will present 1) an overview of current research on release of nanomaterials from nanocomposites by mechanical and environmental stresses, 2) present NIST research on nanomaterial release during exposure to UV environment, and 3) discussed mechanisms of nanomaterial release during UV irradiation of nanocomposites. Nanocomposite specimens were exposed to a NIST integrating SPHERE UV chamber where radiation intensity, temperature,

and relative humidity were well controlled. Specimens irradiated at various UV doses were characterized for chemical degradation, surface morphological changes, nanomaterial accumulation on nanocomposite surface, and amounts of nanomaterial release. The quantities of nanomaterial release and accumulation on composite surface with UV dose were measured by inductively coupled plasma–optical emission spectrometry (ICP-OES). The results showed that photodegradation of the matrix causes a gradual accumulation of nanomaterials on the nanocomposite surfaces. Silica nanoparticles subsequently released to the environment, but MWCNTs formed an entangled network on the nanocomposite surface, with no evidence of release. Mechanisms of nanosilica release and network aggregation of MWCNTs on the composite surface as a function of UV dose will be discussed.

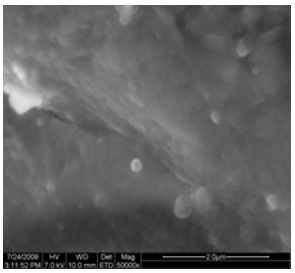

Figure 1: SEM image of the nanomaterial collector surface for epoxy/nanosilica composite after 43 day irradiation with UV, showing clearly silica nanoparticles were released from the nanocomposite.

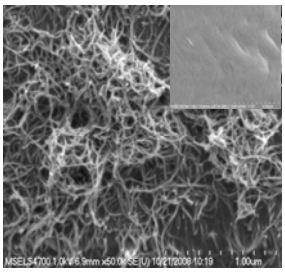

Figure 2: SEM image of epoxy/MWCNT composite surface after 43 d irradiation with UV, showing clearly the dense network aggregation of MWCNTs; the un-irradiated surface was smooth and mostly absent of CNTs, as shown in the inset. image).

III. 質疑応答 (Q&A) [15:10-15:30]

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