

CURRICULUM VITAE

Date: Aug 23, 2016

Name: Tetsuro Hirose, Ph.D.

Address: Institute for Genetic Medicine, Hokkaido University
Kita 15 Nishi 7, Kita-ku, Sapporo 060-0815, Japan

Date of Birth: January 12, 1969

Citizenship: Japanese

<u>Education:</u>	Field of Study	Degree	Year
Nagoya University (Japan)	Molecular Biology	Ph.D.	1995

Carrier:

2013-present	Professor Institute for Genetic Medicine Hokkaido University (Japan)
2012-2013	Group Leader Biomedical Research Institute National Institute of Advanced Industrial Science and Technology (Japan)
2005-2012	Team Leader Biomedical Information Research Center National Institute of Advanced Industrial Science and Technology (Japan)
2004-2007	PRESTO program researcher Japan Science and Technology Agency (Japan)
1999-2004	Postdoctoral fellow in Joan A Steitz's laboratory (HFSP long term fellowship) Howard Hughes Medical Institute, Yale University School of Medicine (USA)
1995-1999	Research Assistant Professor Center for Gene Research Nagoya University (Japan)

5 Selected publications

- Mannen T, Yamashita S, Tomita K, Goshima N, Hirose T. The Sam68 nuclear body is composed of two RNase-sensitive substructures joined by the adaptor HNRNPL. **J. Cell Biol.** 214: 45-59 (2016).
- Kawaguchi, T., Tanigawa, A., Naganuma, T., Ohkawa, Y., Souquere, S., Pierron, G., Hirose, T. SWI/SNF chromatin-remodeling complexes function in noncoding RNA-dependent assembly of nuclear bodies. **Proc. Natl. Acad. Sci. USA.** 112: 4304-4309 (2015).
- Naganuma T, Nakagawa S, Tanigawa A, Sasaki YF, Goshima N, Hirose T. Alternative 3'-end processing of long noncoding RNA initiates construction of nuclear paraspeckles. **EMBO J.** 31, 4020-4034 (2012).
- Sasaki YT, Ideue T, Sano M, Mitsuyama T, Hirose T. MEN ϵ/β noncoding RNAs are structural integrator of the nuclear body, paraspeckle. **Proc. Natl. Acad. Sci. USA.** 106, 2525-2530. (2009).
- Ideue T, Sasaki YT, Hagiwara M, Hirose T. Introns play an essential role in splicing-dependent formation of the exon junction complex. **Genes Dev.** 21, 1993-1998. (2007).

Functional characterization of architectural RNA species toward noncoding RNA taxonomy

Tetsuro Hirose

Institute for Genetic Medicine, Hokkaido University, Sapporo 060-0815, Japan

Numbers of long noncoding RNAs (lncRNAs) have been identified as the structural scaffold of certain membraneless nuclear bodies. They are termed as “architectural RNAs (arcRNAs)” that can be categorized as a distinct subclass of lncRNAs. The arcRNAs function to construct massive nuclear bodies with multiple RNA-binding proteins that possess characteristic prion-like domains (PLDs). The nuclear body formation likely proceeds via liquid-liquid phase separation (LLPS) where arcRNA may locally concentrate multiple PLD proteins to trigger LLPS. However, it remains poorly understood the mechanism how arcRNA is able to concentrate specific sets of PLD proteins. Here, we attempted to identify the functional RNA elements required for nuclear body formation that were embedded in lncRNA sequences using the CRISPR/Cas9 technology and human haploid cell line. We employed human NEAT1 arcRNA required for formation of a nuclear body called paraspeckle. We established over 100 clones that lack portions of the NEAT1 and examined their phenotypes by monitoring paraspeckle integrity. Several clones lacking the specific NEAT1 regions showed remarkable defects in paraspeckle formation, some of which exhibited marked decrease of NEAT1 level and the deletion of the middle part of NEAT1 (Δ middle) caused dispersed paraspeckles, suggesting that this region is required for the formation of higher order paraspeckle structure. Electron- and super resolution-microscopy confirmed the aberrantly dispersed paraspeckle structure and marked diminishment of recruitment of the essential PLD-proteins in Δ middle cells. These data suggest that NEAT1 arcRNA possesses several functionally distinct RNA elements that function with the PLD-containing RNA-binding proteins for nuclear body construction. Furthermore, we recently identified additional arcRNA candidates which commonly exhibited unusual semi-extractable feature during canonical RNA preparation, suggesting the presence of common mechanism(s) underlying the function of multiple arcRNAs.

