

先端研究助成基金助成金(最先端・次世代研究開発支援プログラム) 実績報告書

本様式の内容は一般に公表されず

研究課題名	細胞分化に関与するノンコーディングRNAの全ゲノム解析
研究機関・ 部局・職名	独立行政法人理化学研究所 ライフサイエンス技術基盤研究センター トランスクリプトーム研究チーム チームリーダー
氏名	カルニンチ ピエロ

1. 研究実施期間 平成23年2月10日～平成26年3月31日

2. 収支の状況

(単位:円)

	交付決定額	交付を受けた額	利息等収入額	収入額合計	執行額	未執行額	既返還額
直接経費	138,000,000	138,000,000	0	138,000,000	137,998,147	1,853	0
間接経費	41,400,000	41,400,000	0	41,400,000	41,400,000	0	0
合計	179,400,000	179,400,000	0	179,400,000	179,398,147	1,853	0

3. 執行額内訳

(単位:円)

費目	平成22年度	平成23年度	平成24年度	平成25年度	合計
物品費	133,202	24,630,452	20,873,771	35,212,638	80,850,063
旅費	106,786	2,949,048	2,460,184	503,575	6,019,593
謝金・人件費等	0	17,957,576	18,753,283	13,099,647	49,810,506
その他	0	703,346	424,015	190,624	1,317,985
直接経費計	239,988	46,240,422	42,511,253	49,006,484	137,998,147
間接経費計	0	14,201,400	12,773,100	14,425,500	41,400,000
合計	239,988	60,441,822	55,284,353	63,431,984	179,398,147

4. 主な購入物品(1品又は1組若しくは1式の価格が50万円以上のもの)

物品名	仕様・型・性能等	数量	単価 (単位:円)	金額 (単位:円)	納入 年月日	設置研究機関名
				0		
				0		
				0		

5. 研究成果の概要

We have deeply profiled the transcriptomes of mammalian stem cells and detected Non-Annotated-Stem-Transcript. These noncoding RNAs are rare, lowly conserved and nuclear transcripts found strongly associated with LTR retrotransposons in both human and mouse. We showed that several these LTR-associated RNAs are involved in the maintenance of pluripotency. In addition, we described the recruitment of LTR retrotransposons, in human and mouse, to be part of stem specific enhancer elements implicated in chromatin remodeling and cell cycle regulations.

Although there are not yet direct applications of these findings for regenerative medicine, our findings provide essential information to create better types of cells in future regenerative medicine studies.

課題番号	LS127
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先端研究助成基金助成金(最先端・次世代研究開発支援プログラム) 研究成果報告書

本様式の内容は一般に公表されます

研究課題名 (下段英語表記)	細胞分化に関与するノンコーディング RNA の全ゲノム解析
	Genome-wide identification of non-coding RNA function for cell differentiation
研究機関・部局・ 職名 (下段英語表記)	独立行政法人理化学研究所 ライフサイエンス技術基盤研究センター トランスクリプトーム研究チーム チームリーダー
	RIKEN, Center for Life Science Technologies Transcriptome Technology Team, Team Leader
氏名 (下段英語表記)	カルニンチ ピエロ
	Carninci, Piero

研究成果の概要

(和文):

私たちは哺乳類の幹細胞のトランスクリプトームについて詳しく解析を行い、これまで知られていなかった幹細胞特異的な転写産物(NAST)を発見しました。これらのノンコーディング RNA は発現レベルの低い核 RNA で、ヒト-マウス間では転写産物に類似性のあまりない種特異的な RNA ながら、ヒトおよびマウスそれぞれにおいて LTR レトロトランスポゾンと強く関係していることが分かりました。私たちは LTR に関係する一部の RNA が多能性の維持に関与していることを証明すると共に、ヒトおよびマウスにおいて LTR レトロトランスポゾンがクロマチン再構築および細胞周期の調節に係る、幹細胞特有のエンハンサー要素の一部となることを示しました。

まだこれらの発見は再生医療に直接応用されていませんが、私たちの発見は、将来の再生医療研究において、よりよい細胞を準備するために欠かせない情報を提供することになります。

(英文):

We have deeply profiled the transcriptomes of mammalian stem cells and detected Non-Annotated-Stem-Transcript. These noncoding RNAs are rare, lowly conserved nuclear transcripts found strongly associated with LTR retrotransposons in both human and mouse.

We showed that several LTR-associated RNAs are involved in the maintenance of pluripotency. In addition, we described the recruitment of LTR retrotransposons, in human and mouse, to be part of stem specific enhancer elements implicated in chromatin remodeling and cell cycle regulations.

Although there are not yet direct applications of these findings for regenerative medicine, our findings provide essential information to create better types of cells in future regenerative medicine studies.

1. 執行金額 179,398,147 円

(うち、直接経費 137,998,147 円、 間接経費 41,400,000 円)

2. 研究実施期間 平成23年2月10日～平成 26年 3月31日

3. 研究目的

The ncRNAs, the major, uncharacterized fraction of the genome.

The pervasive transcription of mammalian genomes in multiple transcript classes is now a well-accepted observation made possible thanks to high throughput transcriptomics technologies and large consortia efforts from the FANTOM and the ENCODE projects. However, the large long non-coding RNA (ncRNAs) production of mammalian genomes and its implication in biological pathway remain to be fully explored. Long ncRNAs include intergenic ncRNAs, antisense ncRNAs, and retrotransposon elements (RE) derived ncRNAs. We have recently shown that a very large number of RE are used as promoters (>200,000) of ncRNAs or alternative promoters of mRNAs (*Faulkner et al., Nat. Genet., 2009*). Importantly, RE show very specific tissue and developmental stage restricted expression patterns. Particular RE derived ncRNAs are highly expressed in embryonic stem cells (ESC) and switched off upon differentiation (*Cloonan et al., Nat. Meth., 2009*). Massive RE expression is a hallmark of ESC cells (*Santoni et al., Retrovirology, 2012; Macfarlan et al., Nature, 2012*), whereas RE expression is reduced upon differentiation (*Friedli et al., Genome Res., 2014*).

Exploration of ncRNAs functions for cells reprogramming.

Cell programming, like creation of iPS cells or their subsequent differentiation are limited by a largely uncharacterized "epigenome barrier", of which we only know some common effectors (like modified histones, polycomb proteins) and DNA modification (CpG methylation). Although some ncRNAs have been involved in epigenome control (*Gupta et al., Nature, 2010*), the role of most ncRNAs remains unknown.

This proposal aims at filling the existing gap between the discovery of ncRNAs, including those derived from RE elements, their role and function in the cell, as well as their utilization as tools for another emerging big field in modern science, the regenerative medicine.

4. 研究計画・方法

A comprehensive map of the non-coding transcriptome of mammalian stem cells. Using four complementary highthroughput technologies (CAGE, CAGE-scan RNA-seq and small RNA sequencing), we will comprehensively characterize the nuclear, cytoplasmic and chromatin bound transcriptomes of mammalian stem cells, including capped and non-capped as well as polyadenylated and non-polyadenylated transcripts. These transcriptome profiling methods will be applied on a representative set of human and mouse ESC as well as derived induced pluripotent stem cell (iPSC) lines from three different somatic cell types (fibroblasts, lymphocytes B and T).

This large datasets will then deeply analyzed using state of the art bioinformatics tools. Identification of stem specific ncRNAs will be performed using differential expression analyses on nuclear and cytoplasmic data, followed by comparison with numerous tissue and primary cell samples from the FANTOM5 expression atlas (*Forrest et al., Nature, 2014*). Characterization of newly identified stem specific transcripts will be carried out integrating multiple data sources including ChIP-seq (chromatin immuno-precipitation) for histone marks, transcription factors and co-factors as well as GRO-seq (global run-on) and ChIA-PET (chromosome conformation capture including an immune-precipitation step).

Functional characterization of ncRNAs specific of stem cells.

From the transcriptome datasets extensive analysis, we will select ncRNA candidates putatively implicated in the stem state genetic network and experimentally test their functional role by loss and gain of function experiments.

Loss of function screen will be performed using RNAi (*e.g.* siRNA) and RNase-H (*e.g.* anti-sense oligos) to knock-down ncRNA in a mouse iPS model expressing the GFP reporter gene under the control of a *Nanog* promoter (*Okita et al., Nature, 2007*). Decrease in GFP positive cell population will be measured 48 hours post transfection by flow cytometry and decreased in stemness marker genes upon knock-down will be measured by RT-qPCR.

On the other hand, candidate ncRNA cDNAs, confirmed with deep-RACE experiments, will be cloned in over-expressing vectors and transfect in mouse ESC. Treated cells will be culture in differentiation medium for 48 hours, and differentiation progress monitored based on expression of *Nanog*, known to be among the first stem marker gene to show reduced expression upon differentiation.

Additional experiments will be carried out for newly identified ncRNAs with putative implication in the maintenance of pluripotency inferred from knock-down or over-expression experiments. For this purpose, cells treated either with siRNAs or over-expressing vectors will be analyzed by CAGE in order to delineate implication of these ncRNAs in specific regulatory pathways.

5. 研究成果・波及効果

(研究の主な成果)

We have deeply profiled the nuclear and cytoplasmic transcriptomes of human and mouse stem cells,

applying four complementary high-throughput technologies on 11 pluripotent cell lines (ESC and iPS) and 6 differentiated control cell lines. In detail, genome wide transcription start sites (TSSs) activity was defined using Cap Analysis of Gene Expression (CAGE, *Takahashi et al., Nat. Protoc., 2012*). Second, CAGEscan (CAGE combined with paired-end sequencing, *Plessy et al., Nat. Methods, 2010*) and RNA-seq (*Cloonan et al., Nat. Methods, 2008*) were used to generate *de novo* transcript assemblies. Finally, short-RNA - seq data were produced to assess post-transcriptional RNA processing events. Using state of the art bioinformatics tools, we performed integrative analyzes of these large datasets describing at an unprecedented depth the non-coding transcriptome of mammalian stem cells and identifying novel stem cell specific transcripts, which we published in April 2014 (*Fort et al., Nat. Genet., 2014*).

The original use of CAGE technology on RNAs extracted from the nucleus (rather than from the whole cells as commonly used), allowed the detection of 8,873 and 3,042 mouse and human Non-Annotated-Stem-Transcripts (NASTs) respectively. In their vast majority, NASTs were supported by epigenetic marks characteristic of active transcription, found expressed in most of the ESC and iPS cells included in the study. In addition, NASTs are characterized with a very much stem cell specific expression pattern when compared to other biological states in the recently published FANTOM5 expression atlas (*Forrest et al., Nature, 2014*).

We analyzed the NASTs repeat composition and found that their promoters localized more often than expected by chance in specific LTR retrotransposons families. In detail, novel transcripts associated with LTR-ERVK and LTR-MaLR elements appear clearly enriched in mouse stem cells, while they are more often associated with LTR-ERV1 in human.

In summary, our deep transcriptome profiling suggest that the nuclear transcriptome of stem cells is more complex than previously thought and that an important fraction of the newly identified transcriptomics complexity is composed of genes with promoters associated to a few specific types of mouse ERVK and human ERV1 elements.

We have tested implication of NASTs in the maintenance of pluripotency. Lots of function attempts on NASTs were conducted using multiple types of reagents (*i.e.* short interfering RNAs, siRNA and lock nucleic acids antisense oligos, LNA) in order to obtain a reproducible knock-down of some NASTs candidates in mouse iPS carrying a GFP reporter gene under the control of a *Nanog* promoter (*Okita et al., Nature, 2007*). A total of 150 NASTs were tested, 77 of these being associated with LTR-elements and we have reported for four candidates, direct implication in the genetic regulation of the maintenance of pluripotency (*Fort et al., Nat. Genet., 2014*).

In addition, we discovered that thousands of LTR retrotransposons have been recruited, in human as well as in mouse, to be part of stem specific enhancer elements implicated in chromatin remodeling and cell cycle regulations, which are essential functions for stem cells. We identified 1,498 and 217 putative LTR-associated enhancer regions base on characteristic balanced bi-directional transcription patterns. The regulatory potential functions of mouse ERVK and human ERV1 associated loci are supported by an open chromatin configuration specific in ESC as well as binding of core stem transcription factors (*e.g. Nanog, Sox2, Pou5f1*) and the

enhancer co-factor *P300*. Finally, histone mark associated with enhancers (H3K27ac) was clearly enriched at these loci unlike repressive marks (H3K36me3, H3K9me3). Taken together these results suggest that in stem cells some retrotransposons have been recruited as regulatory elements and can be detected as enhancer-RNAs among novel stem cell specific transcripts identified in this study.

Furthermore, we are currently performing over-expression experiments of NAST candidates. 70 NASTs were cloned within an expressing vector and over-expressed in mouse ESC to test for their ability to slow down passive differentiation process, following LIF removal. 10 of them lead to significant slowdown of differentiation, when measuring *Nanog* expression. We are currently performing transcriptome wide analyses following overexpression of 6 of these 10 candidates.

Beside transcriptional exploration of stem cells and function of ncRNAs, we are pursuing the development of technology for the detection of RNA-chromatin interactions. We aim at finding optimal conditions for asymmetric ligation of RNA and DNA using home-made linker. The goal being to obtain cDNA linked to fragmented chromatin pieces, which are isolated together only when ncRNAs are retained on the chromatin. These cDNA/genomic DNA chimeras are then analyzed with next-generation sequencing allowing the construction of a genome-wide map for RNA/chromatin interactions. Our efforts are currently focused on testing different crosslinking approaches as well as optimizing the linker sequences. We have collected preliminary sequencing data confirming the actual production and detection of RNA/DNA chimeras.

(研究の目的に対する達成度)

We are very satisfied with the degree of accomplishment reached within the three years of the project, ultimately leading to the publication of a major paper in *Nature Genetics* (*Fort et al., 2014*). The unexpected finding of such a large un-annotated nuclear transcriptional complexity associated with repeat elements points out to an unpredicted central role for retrotransposons in stem cell biology. We thus chose to focus our effort on the in depth characterization of NASTs.

Still, we have accumulated preliminary data for ncRNA knock-down and over-expression in stem cells. These parts of the project are still ongoing with genome wide experiments aiming at deciphering the mechanism of actions of these transcripts in the mammalian stem cells physiology.

(関連研究分野の進展や国民生活における社会的・経済的な課題解決への波及効果)

We believe that our findings together with other recent reports broadly changed biological paradigm providing a functional role to a part of the “dark matter” of the genome, the non-coding RNAs, including large non-coding RNAs deriving from retrotransposon elements (RE), as well as other sense-antisense and intergenic non-coding transcripts.

The deep transcriptome dataset resulting from our effort, open to the public through the DDBJ repository, will certainly be broadly use by biologist in the field of stem cells and genomics for additional and comparative analyses. We expect a general acceptance that ncRNA have a function and a strategy to show their

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mechanism is shown. It is likely that more colleagues will engage in functional assays by perturbing ncRNAs, including RE element expression.

6. 研究発表等

<p>雑誌論文 計 10 件</p>	<p>(掲載済み一査読有り) 計 10 件</p> <ol style="list-style-type: none"> 1. Fort, A., Hashimoto, K., Yamada, D., Voineagu, I., Salimullah, M., Bonetti, A., Keya, C., Saxena, A., Bertin, N., Kratz, A., Noro, Y., Wong, C., De Hoon, M. J., Andersson, R., Sandelin, A., Suzuki, H., Wei, C., Koseki, H., c the FANTOM5, Hasegawa, Y., Forrest, A.R., <u>Carninci, P.</u> (2014) "Deep transcriptome profiling of mammalian stem cells supports a key regulatory role for retrotransposon in pluripotency maintenance," Nature Genetics, doi: 10.1038/ng.2965 (online). 2. Fadloun, A., Le Gras, S., Jost, B., Ziegler-Birling, C., Takahashi, H., Gorab, E., <u>Carninci, P.</u>, Torres-Padilla M. (2013) "Chromatin signatures and retrotransposon profiling in mouse embryos reveal regulation of LINE-1 by RNA," Nature Structural & Molecular Biology, 20, 332-338. 3. Plessy, C., Desbois, L., Fujii, T., <u>Carninci, P.</u> (2013) "Population transcriptomics with single-cell resolution: a new field made possible by microfluidics: a technology for high throughput transcript counting and data-driven definition of cell types," BioEssays, 35, 131-140. 4. Saxena, A., Tang, D., <u>Carninci, P.</u> (2012) "piRNAs warrant investigation in Rett Syndrome: An Omics Perspective," Disease Markers, 33, 261-275. 5. Francia, S., Michelini, F., Saxena, A., Tang, D., De Hoon, M., Viviana, A., Mione, M., <u>Carninci, P.</u>, D'Adda di Fagnana, F. (2012) "Site-specific DICER and DROSHA RNA products control the DNA damage response," Nature, 488, 231-235. 6. Saxena, A., Wagatsuma, A., Noro, Y., Gurnot, C., Kuji, T., Watahiki, A., Fagiolini, M., Hensch T., <u>Carninci, P.</u> (2012) "TREHALOSE-ENHANCED ISOLATION OF NEURONAL SUB-TYPES FROM ADULT MOUSE BRAIN," BioTechniques, 52, 381-385. 7. Lenhard, B., Sandelin, A., <u>Carninci, P.</u> (2012) "Metazoan promoters: emerging characteristics and insights into transcriptional regulation," Nature Reviews Genetics, 13, 233-245. 8. Plessy, C., Pascarella, G., Bertin, N., Akalin, A., Carrieri, C., Vassalli, A., Lazarevic, D., Severin, J., Vlachouli, C., Simone, R., Faulkner, G., Kawai, J., Daub, C., Zucchelli, S., Hayashizaki, Y., Mombaerts, P., Lenhard, B., Gustincich, S., <u>Carninci, P.</u> (2011) "Promoter Architecture of Mouse Olfactory Receptor Genes," Genome Research, 22, 486-497. 9. Filippo, C. M., Onorati, M. C., Kothe, G. O., Burroughs, A., Parsi, K-M., Breiling, A., Lo Sardo, F., Saxena, A., Miyoshi, K., Siomi, H., Siomi, M. C., <u>Carninci, P.</u>, Gilmour, D. S., Corona, D. F. V., Orlando, V. (2011) "Chromatin-associated RNA interference components contribute to transcriptional regulation in Drosophila," Nature, 480, 391-395. 10. Saxena, A., <u>Carninci, P.</u> (2011) "Long Non coding RNA modifies chromatin," BioEssays," 33, 1-10. <p>(掲載済み一査読無し) 計 0 件</p> <p>(未掲載) 計 0 件</p>
<p>会議発表 計 26 件</p>	<p>専門家向け 計 26 件</p> <ol style="list-style-type: none"> 1. <u>Carninci, P.</u> "The complexity of mammalian transcription," Invited talk at Genomics Core Facility, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom, March 4, 2014, Genomics Core Facility, Guy's and St Thomas' NHS Foundation Trust. 2. <u>Carninci, P.</u> "The complexity of mammalian transcription," "Dahlem Colloquia in Molecular Genetics" seminar series, Max Planck Institute, Berlin, Germany, February 25, 2014, The Student Association of Max Planck Institute for Molecular Genetics. 3. <u>Carninci, P.</u> "Identification of novel long-non-coding RNAs that are important for maintenance of iPS," Small RNAs to Stem Cells & Epigenetic Reprogramming Asia-2013 Meeting, Sanjo Conference Hall, University of Tokyo Hongo Campus, Tokyo, Japan, November 25 to 26, 2013. GeneExpression Systems, Inc. 4. <u>Carninci, P.</u> "The complexity of mammalian transcription," Invited talk at Karolinska Institutete Karolinska Institutete, Stockholm, Sweden, November 19, 2013, Karolinska Institutete. 5. <u>Carninci, P.</u> "The complexity of mammalian transcription," Practical Workshop on High-Throughput Sequencing Data Analysis, Main campus and Seaside House at Okinawa Institute of Science and

	<p>Technology, Okinawa, Japan, September 30 to October 4, 2013, Okinawa Institute of Science and Technology.</p> <p>6. <u>Carninci, P.</u> "The complexity of mammalian transcription," 2013 RiboClub Annual Meeting, Hôtel Chéribourg, Quebec, Canada, September 23 to 25, 2013, RiboClub Society.</p> <p>7. <u>Carninci, P.</u> "Complexity of mammalian Transcription...as a paradigm in decision making in science," BrainTrain workshop RIKEN Yokohama, Yokohama, Japan, September 16 to 20, 2013, BrainTrain and Center for Life Science Technologies, RIKEN.</p> <p>8. <u>Carninci, P.</u> "The complexity of mammalian transcription," The Fukuoka International Symposium on Genomics & Epigenomics 2013 -Expanding Frontiers of Genomics Science, Kyushu University, Fukuoka, Japan, September 10, 2013, Kyushu University.</p> <p>9. <u>Carninci, P.</u> "The complexity of mammalian transcription," Annual Genetics and Genomics BioConference Live (Webinar) Online, Yokohama, Japan, August 23, 2013, LabRoots, Inc.</p> <p>10. <u>Carninci, P.</u> "Complexity of mammalian transcription," The 34th Annual Lorne Genome Conference 2013, Lorne, Victoria, Australia, February 18, 2013, The LorneGenome 2013 Organising Committee.</p> <p>11. <u>Carninci, P.</u> "Complexity of mammalian transcription," International Society for Commutational Biology – Asia and the ShenZhen Conference on Computational Genomics (ISCB-Asia/SCCG) 2012, Kingkey Palace Hotel, Shenzhen, China December 17, 2012, ISCB-Asia/SCCG.</p> <p>12. <u>Carninci, P.</u> "The complexity of mammalian transcription," 第 35 回日本分子生物学会年会; The 35nd Annual Meeting of the Molecular Biology Society of Japan (MBSJ) Fukuoka International Congress Center / Marinemesse Fukuoka, Fukuoka, Japan December 11, 2012, MBSJ.</p> <p>13. <u>Carninci, P.</u> "Miniaturization of CAGE technologies towards single cell profiling," The 2nd Annual BioTechniques "Virtual" Symposium (Webinar) Online, Yokohama, Japan October 24, 2012, Bio Techniques.</p> <p>14. Ghosheh, Y., Ryu, T., Clinton, M., <u>Carninci, P.</u>, Faulkner, G., Ravasi T. "Genome-wide discovery of piRNA clusters dynamically regulated during brain development," ECCB'12 - the European Conference on Computational Biology 2012, Congress Center Basel, Basel, Switzerland, September 9, 2012, the SIB Swiss Institute of Bioinformatics, Biozentrum University of Basel, and SystemsX.ch.</p> <p>15. Iwasaki, Y., Sato, K., Shibuya, A., Kamatani, M., Tsuchizawa, Y., <u>Carninci, P.</u>, Siomi, H., Siomi, M. "An essential role of a Tudor domain-containing protein, Krimper, in Drosophila piRNA biogenesis," Regulatory & Non-Coding RNAs, Cold Spring Harbor Laboratory, New York, United States, August 28, 2012.</p> <p>16. <u>Carninci, P.</u> "A brief introduction to proteome complexity using high-throughput transcriptome data," The Japan Human Proteome Organization 2012 Annual Meeting / 日本プロテオーム学会 2012 年大会 (10thJHUPO) Miraikan, Tokyo, Japan, July 26, 2012, Japan Human Proteome Organization.</p> <p>17. Iwasaki, Y., Sato, K., Shibuya, A., Komai, M., <u>Carninci, P.</u>, Siomi, H., Siomi, M. "An essential role of a Tudor domain-containing protein, Krimper, in piRNA mediated transposable element silencing in Drosophila germline," ISSCR Annual Meeting, Pacifico Yokohama, Yokohama, Japan, June 13, 2012, International Society of Stem Cell Research.</p> <p>18. <u>Carninci, P.</u> "Discovery of the RNA world and new biotechnology opportunities," Discovery of the RNA World and New Biotechnology Opportunities at ACCJ, ACCJ Tokyo Office, Tokyo, Japan, June 7, 2012.</p> <p>19. <u>Carninci, P.</u> "The complexity of the mammalian transcriptome," Inserm workshop 215 "Diversity of non coding transcriptomes revealed by RNA-seq," Hotel Mercure Bordeaux Centre, Bordeaux, France, May 31, 2012.</p> <p>20. <u>Carninci, P.</u> "Complexity of the mammalian transcriptome," SRP Diabetes Mini Symposium at Karolinska Institute, Karolinska Institute, Stockholm, Sweden May 29, 2012.</p> <p>21. <u>Carninci, P.</u> "Complexity of mammalian transcription analyzed by DeepCAGE," Keystone Symposium on Non-Coding RNAs, Snowbird Resort , Snowbird, Utah, United States, April 1, 2012, Keystone Symposia on Molecular and Cellular Biology .</p> <p>22. <u>Carninci, P.</u> "Complexity of mammalian transcription analyzed by DeepCAGE," Functional Genomics & Systems Biology 2011, Wellcome Trust Conference Centre, Wellcome Trust Genome Campus, Hinxton, Cambridge, United Kingdom, November 29, 2011, The Wellcome Trust.</p> <p>23. <u>Carninci, P.</u> "The complexity of mammalian transcription," Talk at Stazione Zoologica 2011 Annual Seminar Series, The Stazione Zoologica, Naples, Italy, November 28, 2011.</p> <p>24. <u>Carninci, P.</u> "Complexity of mammalian transcription analyzed by DeepCAGE," Cold Spring Harbor</p>
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	<p>Conferences Asia: Bioinformatics of Human and Animal Genomics, Suzhou Dushu Lake Conference Center, Suzhou, China, November 14, 2011.</p> <p>25. <u>Carninci, P.</u> "The complexity of the mammalian transcriptome," Theo Murphy International Scientific Meeting, Kavli Royal Society International Centre, Chicheley Hall, Buckinghamshire, United Kingdom, September 19, 2011.</p> <p>26. Davis, C. Chakraborty, S., Lin, W., Hoon-See, L., Wang, H., Dobin, A., Lassmann, T., Hayashizaki, Y., <u>Carninci, P.</u>, Gingeras, T. "The Diversity of Human Small RNAs," The Biology of Genomes (2011), Cold Spring Harbor Laboratory, New York, United States, May 10, 2011.</p> <p>一般向け 計 0 件</p>
図書 計 1 件	<p>Harbers, Matthias and Carninci, Piero (2013) "Noncoding RNA: The Major Output of Gene Expression," Jane Wu (ed.), <i>Post-transcriptional Gene Regulation: RNA processing in eukaryotes</i>, Wiley-Blackwell, 181-2013. ISBN 978-3-527-32202-2</p>
産業財産権 出願・取得 状況 計 1 件	<p>(取得済み) 計 1 件 Functional nucleic acid molecule and use thereof; <u>P. Carninci</u>, A. Forrest, S. Gustincich, C. Carrieri, S. Zucchelli, PCT Pub. No. WO 2012/133947</p> <p>(出願中) 計 0 件</p>
Webページ (URL)	<p>理化学研究所 ライフサイエンス技術基盤研究センター 機能性ゲノム解析部門 http://www.clst.riken.jp/activity/functionalgenomics.html</p>
国民との科学・技術対話の実施状況	<p>1. 横浜サイエンスフロンティア高等学校第 5 回文化祭への出展(セントラル・ドグマについての3D映画の放映、遺伝子およびセントラル・ドグマについてのパネル展示)、2013年9月21&22日、横浜サイエンスフロンティア高等学校(対象:文化祭参加者)</p> <p>2. 横浜サイエンスフロンティア高等学校第 4 回文化祭への出展(セントラル・ドグマについての3D映画の放映、遺伝子およびセントラル・ドグマについてのパネル展示)、2012年9月15&16日、横浜サイエンスフロンティア高等学校(対象:文化祭参加者)</p> <p>3. <u>Carninci, P.</u> "ゲノムってどうやって調べるの? どう役に立つの?" RIKEN Yokohama Science Café (理研よこはまサイエンスカフェ), Yokohama City Central Public Library (中央図書館), Yokohama, Japan March 4, 2012 (対象:横浜市民、定員:40名)</p>
新聞・一般雑誌等掲載 計 2 件	<p>1. 読売新聞朝刊「学ぶ育むわかるサイエンス ヒトゲノム解読苦悩の 10 年」26 頁(2013 年 5 月 5 日)</p> <p>2. Newton2013 年 5 月号、2013 年 3 月 26 日、pp.44-63、「あなたは究極の個人情報を手に入れたいか? 新・ゲノム革命」</p>
その他	<p>「ヒトゲノムの 80% に機能解析プロジェクト「ENCODE」が解明」、理化学研究所、http://www.riken.jp/pr/press/2012/20120906/</p>

7. その他特記事項