Int. J. Dev. Biol. 52: 377-381 (2008)
doi: 10.1387/ijdb.072389ns

THE INTERNATIONAL JOURNAL OF DEVELOPMENTAL BIOLOGY
www.intjdevbiol.com

Expression of zinc transporter family genes in *Dictyostelium*

NOBUYA SUNAGA[#], MERI MONNA, NAO SHIMADA, MAI TSUKAMOTO and TAKEFUMI KAWATA[*]

[1]*Department of Biology, Faculty of Science, Toho University, Funabashi, Chiba, Japan*

ABSTRACT Regulation of the zinc ion concentration is physiologically important to control the activities of a variety of cellular molecules. A BLAST search against a conserved domain of known zinc transporters identified twelve putative zinc transporter family genes in the *Dictyostelium* genome. Phylogenetic analysis revealed the presence of three zinc transporter subfamilies in *Dictyostelium*. One subfamily of proteins, consisting of the ZntA-D proteins, has weak homology to the STAT3-inducible LIV-1 protein. In addition, *in situ* hybridization revealed that the *zntA-D* genes are expressed in the pstAB cells, this expression being absent in the *Dd-STATa* null mutant. Thus, Dd-STATa may control stalk cell differentiation through some members of the zinc transporter family genes during *Dictyostelium* development.

KEY WORDS: *STAT transcription factor, zinc transporter, cell differentiation, Dictyostelium*

The JAK/STAT signaling pathways are induced by cytokines and growth factors and play indispensable roles in controlling the immune system, cell fate determination, and cell proliferation in an evolutionarily conserved manner (Darnell, 1997; O'Shea *et al*., 2002; Rawlings *et al*., 2004). Protozoan cellular slime mould, *Dictyostelium discoideum*, possesses functional homologs of the metazoan STAT genes, *Dd-STATa-d* (Kawata *et al.,* 1997; Fukuzawa *et al.,* 2001; Zhukovskaya *et al.,* 2004; Gao *et al.,* 2004). The *Dd-STATa*'null strain has defects in both chemotactic cell movements during the aggregation stage and morphogenesis during late development, and the latter defect leads to a failure of culmination (Mohanty *et al*., 1999). Thus, Dd-STATa is necessary for the entry into culmination that accompanies proper conversion of prestalk cells into stalk cells.

In *Dictyostelium*, the conversion of isolated prestalk cells into stalk cells *in vitro* is enhanced by zinc ions in the presence of DIF-1, a differentiation-inducing factor (Kubohara and Okamoto, 1994; Kubohara, 1995). This observation indicates that exogenous zinc ions may have an important role in stalk differentiation, although the mechanism of zinc action remains unclear. STAT3 controls EMT (epithelial-mesenchymal transition) through the LIV-1 protein during zebrafish gastrulation (Yamashita *et al*., 2004). STAT3 is activated in the organizer region and'activates transcription of the LIV-1 gene, which encodes a zinc transporter protein (McClelland *et al*., 1998). LIV-1 induces nuclear transition of the zinc finger protein Snail, which is a main regulator of EMT and is a transcriptional repressor of the E-cadherin gene encoding a cell adhesion molecule (Batlle *et al.,* 2000; Cano *et al.,* 2000). Because the *Dd-STATa* null strain lacks an organizer-like activity, if LIV-1-related molecules are present in *Dictyostelium*, then they could be regulated by Dd-STATa and may have crucial roles during fruiting body formation.

There are two zinc transporter families in eukaryotes, the CDF (Cation Diffusion Family) and the ZIP (Zrt, Irt-like Proteins) family, the latter family includes LZT (LIV-1 subfamily of ZIP zinc Transporters). While CDF is responsible for zinc transport from the cytoplasm to either intracellular organelles or extracellular spaces, the ZIP family is important for transferring zinc from the extracellular space into the cytoplasm (Taylor and Nicholson, 2003; Liuzzi and Cousins, 2004). The ZIP transporter family consists of four subfamilies: I, II, gufA, and LZT (Gaither and Eide, 2001). The LZT subfamily is distinguished from the other ZIP subfamilies by the presence of the HEXPHEXGD motif in the fifth transmembrane region. This motif is less conserved in other zinc transporter proteins (Taylor and Nicholson, 2003).

To identify putative zinc transporters in *Dictyostelium*, we searched the amino acid sequences of Zrt, Irt, and ZIP proteins (ZIP subfamilies I and II), LIV-1 and KE4 proteins (LZT subfamily), and ZnT protein (CDF family) against the entire genomic sequence of *Dictyostelium* by using the BLAST program. The search identified 12 putative zinc transporter family genes in *Dictyostelium* (Table 1). Phylogenetic analysis showed that these

***Address correspondence to:** Takefumi Kawata. Department of Biology, Faculty of Science, Toho University, 2-2-1 Miyama, Funabashi, Chiba 274-8510, Japan. e-mail: tkawata@bio.sci.toho-u.ac.jp

[#]**Present address:** Department of Biological Sciences, Graduate School of Science, Tokyo Metropolitan University, Minami-Ohsawa 1-1, Hachioji, Tokyo 192-0397, Japan.

Accepted: 7th September 2007. *Published online:* 26th December 2007.

0214-6282/2008/$35.00

Printed in Spain
www.intjdevbiol.com

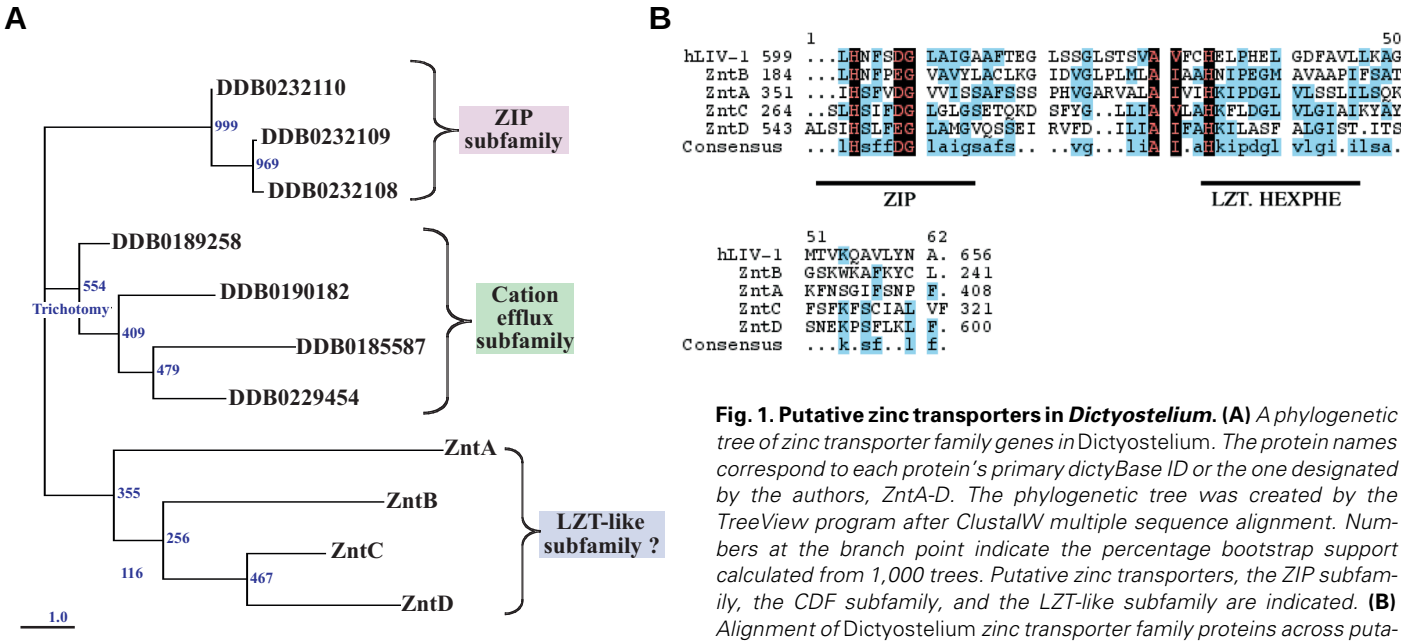


Fig. 1. Putative zinc transporters in *Dictyostelium*. (A) *A phylogenetic tree of zinc transporter family genes in* Dictyostelium. *The protein names correspond to each protein's primary dictyBase ID or the one designated by the authors, ZntA-D. The phylogenetic tree was created by the TreeView program after ClustalW multiple sequence alignment. Numbers at the branch point indicate the percentage bootstrap support calculated from 1,000 trees. Putative zinc transporters, the ZIP subfamily, the CDF subfamily, and the LZT-like subfamily are indicated.* **(B)** *Alignment of* Dictyostelium *zinc transporter family proteins across putative transmembrane domains IV and V. Amino acid sequences of human LIV1 and* Dictyostelium *ZntA, ZntB, ZntC, and ZntD were aligned by the MultAlin program (Corpet, 1988; http://prodes/toulouse.inra.fe/multalin). Amino acid residues identical among more than 80% of the family members are shown with pink in black, and residues identical among more than 40%, but less than 80%, of the family members are shaded in pale blue. Positions of amino acid position numbers are shown at both ends. ZIP means the position where is a ZIP conserved sequence (GIVXHSVIIGLSL) in the transmembrane domain IV of ZIP subfamily, while LZT.HEXPHE is the conserved motif of the LZT subfamily in the transmembrane domain V (Taylor and Nicholson, 2003).*

genes were classified into three groups (Fig. 1A).

Among the 12 genes, the *DDB0232108* (*=DDB0217318*), *DDB0232109* and *DDB0232110* genes were predicted to encode ZIP proteins according to their relatively strong homology to *Oryza sativa* ZIP1 (data not shown); thus, they seem to belong to the ZIP subfamily (Fig. 1A). A database search using the amino acid sequence of CDF protein identified four genes, *DDB0189258*, *DDB0190182*, *DDB0185587,* and *DDB0229454*. Gene ontology annotations predicted that they encode cation transporters. Thus, they appear to belong to the CDF subfamily (Fig. 1A).

BLAST searches using amino acid sequences derived from LZT proteins identified *DDB0202214*, *DDB0218806*, *DDB0186791*, and *DDB0190179* genes. We designated these genes as *zntA*, *zntB*, *zntC*, and *zntD*, respectively. ZntA-D proteins have less similarity to *O. sativa* ZIP1 than supposed *Dictyostelium* ZIP subfamily proteins have (data not shown). The predicted HEXPHEXGD-like motifs found in their fifth putative transmembrane region (Fig. 1B; Fig. 2, shaded sequences) have very weak homology to the human LIV-1 protein; rather, they show some homologies to ZIP subfamily proteins. However, they still likely belong to a subfamily closer to LZT than to the ZIP or CDF subfamilies. When the amino acid sequences across putative transmembrane domains IV and V of ZntA, B, C, and D are compared to that of human LIV-1 (Fig. 1B), the first X in the HEXPHEXGD motif is either leucine or isoleucine for the LZT subfamily, while X is phenylalanine for almost all ZIP and CDF subfamilies (Taylor and Nicholson, 2003). Except for ZntC, the others have isoleucine at the same position. The second X is leucine for almost all of the LZT subfamily and is conserved in ZntA and ZntC. In addition, ZntA and ZntB possess a proline

TABLE 1

SUMMARY OF ZINC TRANSPORTER FAMILY GENES IN *DICTYOSTELIUM*

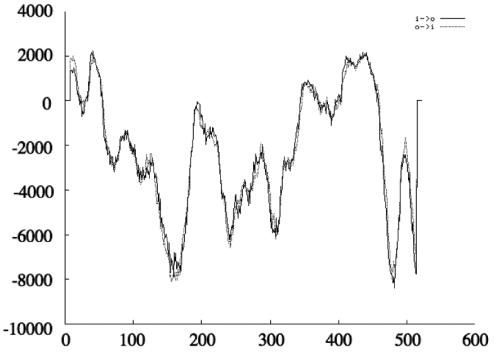
Protein Name (primary dictyBaseID)	EST clone	Gene Name	Chromosome	Amino Acids	Aligned Score to ZntA
DDB0232109*			#2	375	14
DDB0232108			#2	389	10
DDB0232110			#3	371	14
DDB0218806	*SFB676*	*zntB*	#4	372	12
DDB0186791	*SSK308, dds13d1*	*zntC*	#4	401	20
DDB0202214	*SSH647, dds31e08*	*zntA*	#1	523	100
DDB0190179		*zntD*	#1	683	22
DDB0189258			#5	770	12
DDB0190182			#1	614	11
DDB0185587	*SLC791*		#4	543	16
DDB0229454	*SLF290*		#3	572	8

* There is a duplicated gene (*DDB0217318*) in strains Ax3 and Ax4 (but not Ax2).

Fig. 2 (Opposite). Predicted amino acid sequences of zinc transporter proteins and hydrophobicities. *Predicted amino acid sequences of ZntA-ZntD are shown to the left. Thick lines indicate the putative transmembrane domains (TM I-VII). The sequences with weak homology to the conserved HEXPHEGDFA motif of the LZT subfamily are shaded. Hydrophobicity profiles were created by TMpred (http://www.ch.embnet.org/software/TMPRED_form.html) with default setting (Hofmann and Stoffel, 1993). Two orientations are possible and both models are shown: one is in-out direction (shown as normal line) and the other is out-in direction (shown as dotted line). Horizontal axis denotes the amino acid number of the predicted protein; the longitudinal axis denotes the hydrophobicity where plus number means hydrophobic.*

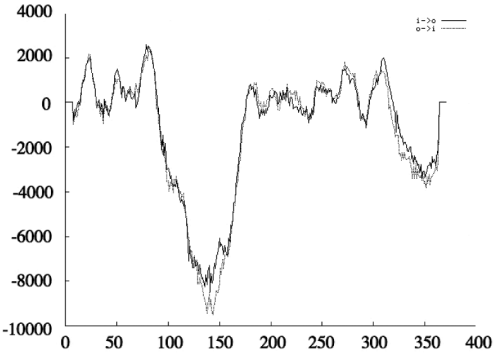
ZntA

```
1    MSIFAYSILAGLAPLLSSSIPFFTLRNRNINASVFHILLCISAGLLFAVASLELIPESMNLALRSFEESTKTQTSLKSTTT
                TM I                      TM II                    TM III
82   KTTTTTTTIGNIKLQKSFISNSEDSLNEFHSLDNEINKPPIEGLNLNNLNQATNLDNNEEDNDNLDNDGENEIENDHDHDH

163  QEDEGGDNDHDHESEEKKEFLKIPMYGIGSIDGGGGGGGHHSHSHGSLSSSSSNDVISDYISNNNSNNINNNDDDNNNNNN

244  NNDDDDDSVELLERNVVNKDNSNNINNINNNNDDEDIIVINKSIENTPNIASPVMNKDNNNNDKDKNRNSNKSDIKNSGSI

325  NNGNNSGNNNNNNKSKLTITTFIALSIHSFVDGVVISSAFSSSPHVGARVALAIVIHKIPDGLVLSSLILSQKKFNSGIFS
                        TM IV                          TM  V
406  NPFFYFLLISCMTPLGSFISSFLFGGLSLSSGAFVLGFGAGTFIYITSTAILPEILSNQIIKFDFKKKNLKKKKKKKKKS
              TM  VI                  TM  VII
487  KPKMEKIDAMGNLKLSSFPFRKEIKKKNQNKNKKKKR
```



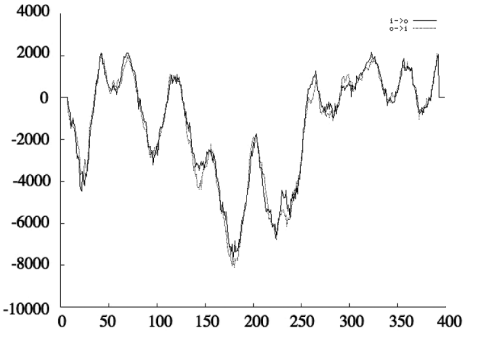
ZntB

```
1    MTSLETYNDNVKTALIMCFLSGLSTAIGGLYVIFIKQQSHKLLGHLLSFSSGVMIYISFMDLLPESIAEIGFYNANIWFFV
                TM I                      TM II                    TM III
82   GIIFFAVILRFVPHDHDESGDSNHAHSHNGASIEKHSSEKKEVVDDDDDDNNGKDKKQKQQKQKQQQQQKQNIAKSKN

163  KKKSKDDYLNSVGIATAGVSLHNFPEGVAVYLACLKGIDVGLPLMLAIAAHNIPEGMAVAAPIFSATGSKWKAFKYCLYSG
                TM IV                          TM  V
244  LCEPVGAIIFGLIFKEYMTPYLIQSMLAAVAGIMVFMVIKELLPAAFKYVSVDESAFSNIIGMIFFFFSIHFLHSMLPHDH
              TM  VI                  TM  VII                  TM  VIII
325  GGAGDGGHGHSHGGHGHSHGHGHSHGGHSHDSQHVESPQSSSFNAFA
```



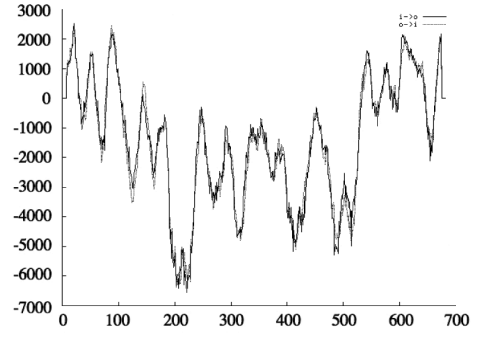
ZntC

```
1    MDIVNDLVSSISSISSEAAEEEAIRDELRNDKGGLIAGIFVLTLTASFVPWFLTKAKITNLVSVVSILTCLSAGVIIGAGF
                                    TM I                      TM II
82   NHILPDAAEEFQSYVEAVAPDNKYGDFPFAHTITIVTMFALICVDKILVSGGLDGEADHNHMDLSQHNHPSPHAAGEIDLN
                        TM III
163  IYTNGDDDDDDVNEDQEEDSTKDDEKEHGHGHGHGHGHNSSNSSSNGHGHGLKKKKKSKKEHGHGHNHDHSSNGHSHKDEK

325  DSEKVNVSSKSKAWVFLVALSLHSIFDGLGLGSETQKDSFYGLLIAVLAHKFLDGLVLGIAIKYAYFSFKFSCIALVFAAA
                TM IV                          TM  V                    TM  VI
406  MTPLGIGIGMAISSAYESSTDAYLVKGIILSITCGSFIYISLIELLPSGLCQKGWPKLKLAVAFLGYSVMAILALWV
                        TM  VII                          TM  VII
```



ZntD

```
1    MGISLSVLDIKIISTTVLFILSLLAGIAPYWMRNLNNSSRYLSWSNTFAGGVFFGAGMLHLFATADEDLQPYVQKYNYPFA
                        TM I                      TM II
82   ALCLCVGFLITLFLELIINSIFIKSNTFASLHGHSHSHVHLSHGHSHHGKDNGSNGNPGSGVGIGMGSVGALNSKKNKTTS
          TM III
163  PTITPTTPSEGTTTTTTTTTATTAATAKEIVLEDEDEDEEKDIMDEIIIPDDYDENDDEQIYKKKQSKCARTKFRKFIDTI

244  PTFSSTSTSSTSSSTKISEKQRLLDSSNSYYYNQNKYKGIIGSHIDIDKSGSGVGGFSNNNNNNNNNNNNNNKNNNNNNNN

325  NFRTEIIIQPISTTSNNSVHHYPSSSVNYHPFITTTTTTCSNDNSNSNNNNSSNNNSSSANITPNTNKILSSSKSLSYRYN

406  GDDEEPDIIIDYDDIDYNQEGRTRGNSLGSDSNVHNERIVLINSGIGNSGNIGSNNNNNNNGGGGGGGGNSNIDYNDNEEN

487  NNNNNKIESEILIKDTTTDSIKNMKGGEHQHQHLHQQEIIVVTKKSNILLPFILVIALSIHSLFEGLAMGVQSSEIRVFDI
                                                    TM IV
568  LIAIFAHKILASFALGISTITSSNEKPSFLKLFLLVFVFSLTSPIGSILGMVIVGSGVTGSMVPPILQGIASGTFLYVAVV
                TM  V                  TM  VI                    TM  VII
648  EIIPKELSHDSDILIKSFLLLLGFSGMAVVAIWV
                        TM  VIII
```



residue that is not found in any ZIP and CDF subfamily proteins. In the transmembrane IV domain, a conserved glycine is next to aspartic acid in LZT, while the glycine is next to isoleucine in most ZIP and CDF subfamily proteins. ZntA-D proteins have acidic residues at the same position (Fig. 1B). This evidence supports the idea that ZntA-D proteins may belong to a subfamily closer to LZT.

To understand the functions of these genes and to clarify whether Dd-STATa regulates their expressions in particular cell types, we compared the expression patterns of *zntA, zntB*, *zntC*, and *zntD* genes in Ax2 and *Dd-STATa* null strains. In the Ax2 strain, all genes were expressed in pstAB cells or at the stalk entrance during culmination (Fig. 3). Both *zntA* and *zntC* genes were expressed in pstAB cells even in the slug stage. There was almost no cell type–specific expression for these genes in the mutant strain, although there was weak expression in the prestalk cells for the *zntC* gene (Fig. 3). These results indicate that Dd-STATa is required for the differentiation of the cell type where zinc transporter family genes are activated. Interestingly, the *zntD* gene was expressed in pstAO cells, a cell type that exists even in the *Dd-STATa* null strain (Mohanty *et al.,* 1999).

The evidence that all four LZT-like zinc transporter family genes are expressed in pstAB cells is important. PstAB cells are strong candidates for "late" organizers during development in *Dictyostelium* (Sternfeld, 1992; Fukuzawa and Williams, 2000; Shimada *et al.,* 2005). PstAB cells are believed to be the location where stalk elongation begins when culmination is started and may provide a signal or the environment for the initiation of terminal stalk cell differentiation. During culmination, prestalk-to-stalk conversion occurs at the stalk tube entrance to differentiate into pstAB cells (Jermyn *et al.,* 1996). Such a conversion is enhanced by zinc ions in the presence of DIF-1 - at least in the *in vitro* monolayer cultured cell condition (Kubohara and Okamoto, 1994; Kubohara, 1995). Serafimidis and Kay (2005) suggested that cadmium (and zinc probably) induces polyketide production. Zinc ions might mimic the action of cadmium ions or some zinc transporters might transport cadmium ions which in turn would result in an elevated level of prestalk and stalk differentiation due to a stimulation of polyketide production. Because the *Dd-STATa* null strain seems to lack pstAB cells and there is almost no expression of the pstAB-specific genes examined so far in the mutant strain (Shimada *et al.,* 2004b; 2005), zinc concentration may be regulated through expression of zinc transporter genes in pstAB cells by Dd-STATa,

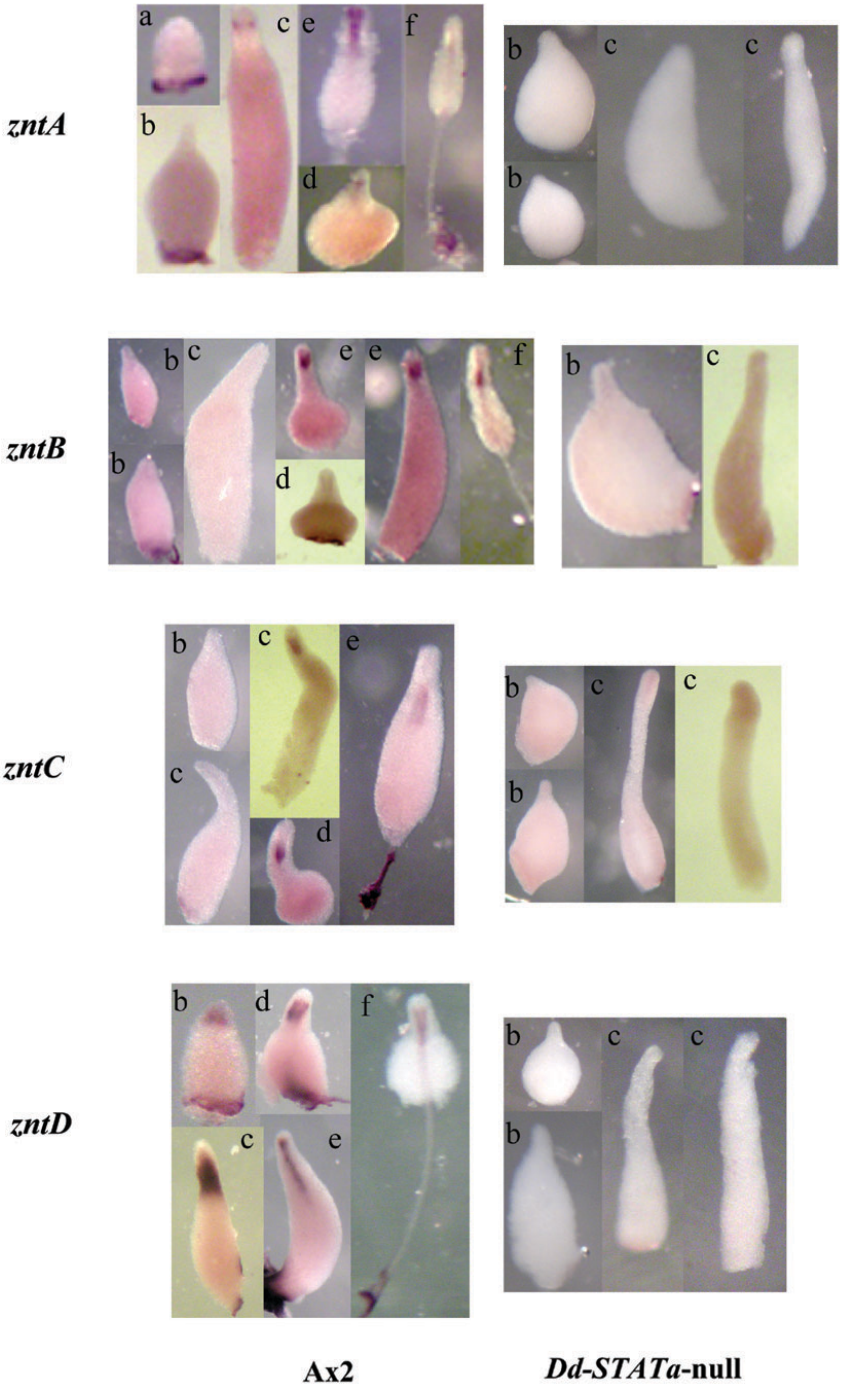


Fig. 3. Comparison of zinc transporter family gene expression in Ax2 and *Dd-STATa* null strains. *The spatial expression pattern of the* zntA-D *genes determined by* in situ *hybridization at the following stages: mound (a), tipped finger (b), slug (c), Mexican hat (d), and culminant (e, f, g) in the Ax2 and* Dd-STATa*-null strains. The dark regions at the base of multicellular structures from several stages of development in zntA-D are supposed to be non-specific slime sheath staining. The RNA probes were synthesized from EST clone dds31e08 for* zntA, *SFB676 for* zntB, *and dds13d1 for* zntC. *For* zntD, *cDNA was amplified, subcloned into pCR-TOPO2.1, and used for probe preparation. The cDNA clones dds31e08 and dds13d1 were provided by Prof. Yuji Kohara, National Institute of Genetics, Japan, as part of the* Dictyostelium *cDNA project.*

although the mode of action by Dd-STATa may be indirect.

Experimental Procedures

Cells and growth conditions

Ax2 and *Dd-STATa* null strains were grown at 22 °C in HL5 medium. *Dd-STATa* null cells were grown in HL5 medium supplemented with blasticidin S (Kaken Pharmaceutical, Tokyo, Japan).

Identification of genes and phylogenetic analysis

Amino acid sequences of ZIP, Znt (Zinc Transporter), and LIV1 proteins were obtained from the National Center for Biotechnology Information (NCBI) database (http://www.ncbi.nih.gov/index.html). To identify zinc transporter family genes in *Dictyostelium*, BLAST searches were performed against the whole genomic sequence of *Dictyostelium* (Dictybase; http://dictybase.org/) using these amino acid sequences. A phylogenetic tree of identified genes was drawn by the TreeViewPPC program (http://taxonomy.zoology.gla.ac.uk/rod/treeview.html) using sequences aligned by the ClustlalW program (http://www.ddbj.nig.ac.jp/search/clustalw-j.html).

In situ *hybridization*

Whole-mount *in situ* hybridization was performed as described previously (Escalante and Loomis, 1995; Maeda *et al*., 2000; 2003; Shimada *et al*., 2004a).

Acknowledgements

This work was partly supported by the Science Special Grant for Promoting Scientific Research at Toho University to T. Kawata (301-12) and by a Grant-in-Aid from the Japanese Society for the Promotion of Science (JSTS) Fellowships for Young Scientists to N. Shimada (#17.2751). N.S. is a JSTS Research Fellow. We thank Prof. Yuji Kohara, National Institute of Genetics, Japan, for providing the cDNA clones.

References

BATLLE, E., SANCHO, E., FRANCI, C., DOMINGUEZ, D., MONFAR, M., BAULIDA, J., and GARCÍA DE HERREROS, A. (2000). The transcription factor snail is a repressor of E-cadherin gene expression in epithelial tumour cells. *Nat. Cell Biol.* 2: 84-89.

CANO, A., PÉREZ-MORENO, M.A., RODRIGO, I., LOCASCIO, A., BLANCO, M.J., DEL, BARRIO, M.G., PORTILLO, F. and NIETO, M.A. (2000). The transcription factor snail controls epithelial-mesenchymal transitions by repressing E-cadherin expression. *Nat. Cell Biol*. 2: 76-83.

CORPET, F. (1988) Multiple sequence alignment with hierarchical clustering. *Nucl. Acids. Res.* 16:10881-10890.

DARNELL, J.E., Jr. (1997). STATs and gene regulation. *Science* 277: 1630-1635.

ESCALANTE, R. and LOOMIS, W.F. (1995). Whole-mount in situ hybridization of cell-type-specific mRNAs in *Dictyostelium*. *Dev. Biol.* 43: 262-266.

FUKUZAWA, M. and WILLIAMS, J.G. (2000). Analysis of the promoter of the *cudA* gene reveals novel mechanisms of *Dictyostelium* cell type differentiation. *Development* 127: 2705-2713.

FUKUZAWA, M., ARAKI, T., ADRIAN, I. and WILLIAMS, J.G. (2001). Tyrosine phosphorylation-independent nuclear translocation of a *Dictyostelium* STAT in response to DIF signaling. *Mol. Cell* 7: 779-788.

GAO, Q., HUA, J., KIMURA, R., HEADD, J.J., FU, X.Y. and CHIN, Y.E. (2004). Identification of the linker-SH2 domain of STAT as the origin of the SH2 domain using two-dimensional structural alignment. *Mol. Cell. Proteomics* 3: 704-714.

GAITHER, L.A. and EIDE, D.J. (2001). Eukaryotic zinc transporters and their regulation. *Biometals.*14:251-270.

HIROKAWA, T., BOON-CHIENG, S. and MITAKU, S. (1998). Sosui: classification and secondary structure prediction system for membrane proteins. *Bioinfomatics* 14: 378-379.

HOFMANN, K. and STOFFEL, W. (1993). TMbase - a database of membrane spanning proteins segments. *Biol. Chem. Hoppe-Seyler.* 347: 166.

JERMYN, K.A., TRAYNOR, D. and WILLIAMS, J.G. (1996). The initiation of basal disc formation in *Dictyostelium discoideum* is an early event in culmination. *Development* 122: 753-760.

KAWATA, T., SHEVCHENKO, A., FUKUZAWA, M., JERMYN, K.A., TOTTY, N.F., ZHUKOVSKAYA, N.V., STERLING, A.E., MANN, M. and WILLIAMS, J.G. (1997). SH2 signaling in a lower eukaryote: A STAT protein that regulates stalk cell differentiation in *Dictyostelium. Cell* 89: 909-916.

KUBOHARA, Y. (1995). Zinc ions promote prestalk-to-stalk and pespore-to-stalk conversions in *Dictyostelium discoideum. FEMS Micorobiol. Lett.* 134: 15-18.

KUBOHARA, Y. and OKAMOTO, K. (1994). Specific induction by zinc of *Dictyostelium stalk* cell differentiation. *Exp. Cell Res.* 214: 367-372.

LIUZZI, J.P., and COUSINS, R.J. (2004). Mammalian zinc transporters. *Annu. Rev. Nutr.* 24: 151-72.

MAEDA, M., KUWAYAMA, H., YOKOYAMA, M., NISHIO, K., MORIO, T., URUSHIHARA, H., KATHO, M., TANAKA, Y., SAITO, T., OCHIAI, H., TAKEMOTO, K., YASUKAWA, H. and TAKEUCHI, I. (2000). Developmental changes in the spatial expression of genes involved in myosin function in *Dictyostelium*. *Dev. Biol*. 43: 114-119.

MAEDA, M., SAKAMOTO, H., MARUO, T., OGIHARA, S., IRANFAR, N., FULLER, D., MORIO, T., URUSHIHARA, H., TANAKA, Y. and LOOMIS, W.F. (2003). Changing patterns of gene expression in *Dictyostelium* prestalk cell subtypes recognised by *in situ* hybridisation with genes from microarray analyses. *Eukaryot. Cell* 2: 638-645.

McCLELLAND, R.A., MANNING, D.L., GEE, J.M., WILLSHER, P., ROBERTSON, J.F., ELLIS, I.O., BLAMEY, R.W. and NICHOLSON, R.I. (1998) Oestrogen-regulated genes in breast cancer: association of pLIV1 with response to endocrine therapy. *Br. J. Cancer* 77: 1653-1656.

MOHANTY, S., JERMYN, K.A., EARLY, A., KAWATA, T., AUBRY, L., CECCARELLI, A., SCHAAP, P., WILLIAMS, J.G. and FIRTEL, R.A. (1999). Evidence that the *Dictyostelium* Dd-STATa protein is a repressor that regulates commitment to stalk cell differentiation and is also required for efficient chemotaxis. *Development* 126: 3391-3405.

O'SHEA, J.J., GADINA, M. and SCHREIBER, R.D. (2002). Cytokine signaling in 2002: New surprises in the Jak/Stat pathway. *Cell* 109: S121-S131.

RAWLINGS, J.S., ROSLER, K.M. and HARRISON, D.A. (2004). The JAK/STAT signaling pathway. *J. Cell Sci.* 117: 1281-1283.

SERAFIMIDIS, I. and KAY, R.R. (2005). New prestalk and prespore inducing signals in *Dictyostelium*. *Dev. Biol.* 282: 432-441.

SHIMADA, N., NISHIO, K., MAEDA, M., URUSHIHARA, H. and KAWATA, T. (2004a). Extracellular matrix family proteins that are potential targets of Dd-STATa in *Dictyostelium discoideum. J. Plant Res.* 117:345-353.

SHIMADA, N. MAEDA, M., URUSHIHARA, H. and KAWATA, T. (2004b). Identification of new modes of Dd-STATa regulation of gene expression in *Dictyostelium* by *in situ* hybridisation. *Int. J. Dev. Biol.* 48: 679-682.

SHIMADA, N. MARUO, T., MAEDA, M., URUSHIHARA, H. and KAWATA, T. (2005). Evidence that the *Dictyostelium* STAT protein Dd-STATa plays a role in the differentiation of inner basal disc cells and identification of a promoter element essential for expression in these cells. *Differentiation* 73: 50-60.

STERNFELD, J. (1992). A study of PstB cells during *Dictyostelium* migration and culmination reveals a unidirectional cell type conversion process. *Roux's Arch. Dev. Biol.* 201: 354-363.

TAYLOR, K.M. and NICHOLSON, R.I. (2003). The LZT proteins; the LIV-1 subfamily of zinc transporters. *Biochim. Biophys. Acta.* 1611: 16-30.

THUSNÁDY, G.E. and SIMON, I. (1998). Principles governing amino acids composition of integral membrane proteins: application to topology prediction. *J. Mol. Biol.* 283: 489-506.

YAMASHITA, S., MIYAGI, C., FUKADA, T., KAGARA, N., CHE, Y.S. and HIRANO, T. (2004). Zinc transporter LIVI controls epithelial-mesenchymal transition in zebrafish gastrula organizer. *Nature* 429: 298-302.

ZHUKOVSKAYA, N.V., FUKUZAWA, M., TSUJIOKA, M., JERMYN, K.A., KAWATA, T., ABE, T., ZVELEBIL, M. and WILLIAMS, J.G. (2004). Dd-STATb, a *Dictyostelium* STAT protein with a highly aberrant SH2 domain, functions as a regulator of gene expression during growth and early development. *Development* 131: 447-458.

Related, previously published *Int. J. Dev. Biol.* articles

See our recent Special Issue ***Ear Development*** edited by Fernando Giraldez and Bernd Fritzsch at: http://www.ijdb.ehu.es/web/contents.php?vol=51&issue=6-7

See our Special Issue ***Mammalian Reproduction & Development*** in honor of Anne McLaren and edited by Brigid Hogan at: http://www.ijdb.ehu.es/web/contents.php?vol=45&issue=3

Analysis of a homologue of the adducin head gene which is a potential target for the Dictyostelium STAT protein Dd-STATa
Ryota Aoshima, Rieko Hiraoka, Nao Shimada and Takefumi Kawata
Int. J. Dev. Biol. (2006) 50: 523-532

Identification of new modes of Dd-STATa regulation of gene expression in Dictyostelium by in situ hybridisation
NAO SHIMADA, MINEKO MAEDA, HIDEKO URUSHIHARAand TAKEFUMI KAWATA
Int. J. Dev. Biol. (2004) 48: 679-682

Expression and role of adenylyl cyclases during late development in Dictyostelium discoideum
E Alvarez-Curto, ME Meima, P Schaap
Int. J. Dev. Biol. (2001) 45: S147-S148

The MADS-box transcription factor SRFA regulates different aspects of Dictyostelium discoideum development
N Moreno, JJ Vicente, R Escalante, L Sastre
Int. J. Dev. Biol. (2001) 45: S117-S118

Cell cycle phase, cellular Ca2+ and development in Dictyostelium discoideum.
M Azhar, P K Kennady, G Pande, M Espiritu, W Holloman, D Brazill, R H Gomer and V Nanjundiah
Int. J. Dev. Biol. (2001) 45: 405-414

Dictyostelium discoideum: a model system for differentiation and patterning.
R Escalante and J J Vicente
Int. J. Dev. Biol. (2000) 44: 819-835

Cell-cell signaling and adhesion in phagocytosis and early development of Dictyostelium.
E Bracco, B Pergolizzi, B Peracino, E Ponte, A Balbo, A Mai, A Ceccarelli and S Bozzaro
Int. J. Dev. Biol. (2000) 44: 733-742

A cell type-specific effect of calcium on pattern formation and differentiation in dictyostelium discoideum.
R Baskar, P Chhabra, P Mascarenhas and V Nanjundiah
Int. J. Dev. Biol. (2000) 44: 491-498

2006 ISI **Impact Factor = 3.577**