

UNIVERSITÄT LEIPZIG

Fakultät für Mathematik und Informatik

Lehrstuhl für Bioinformatik



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Doctoral research proposal:
Evolution of microRNAs: a comprehensive study
to trace the microRNA ancient origin

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Why is it important to study ancestral microRNA origins?

- The importance of these molecules are coming into focus as more miRNAs and their regulatory targets and functions are discovered
- There are critical questions remain to be answered: its function and its evolution



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The problem could be understood by two basic components

- **Function:** It is extremely interesting the importance of these molecules in modulating some processes of development among plants and animals.
- **Evolution:** Origin of the development nowadays is the utmost importance to trace the origin of multicellularity.



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Relations between two processes

Origins of development

Origins of multicellularity

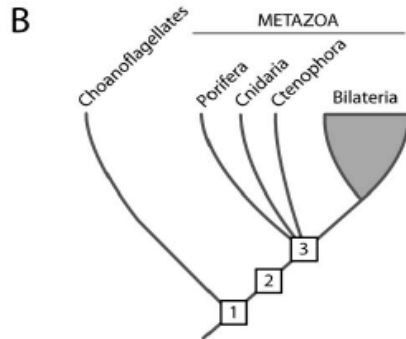
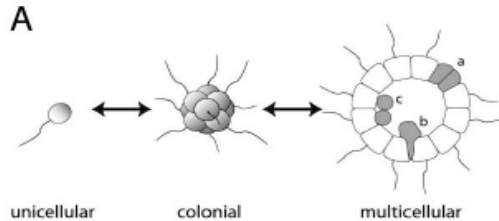


Figure 1. Stages in the Transition to Multicellularity

miRNA function

miRNAs play key roles in the regulation of developmental processes (animal and plants)



miRNAs might be key players in the evolution of developmental processes

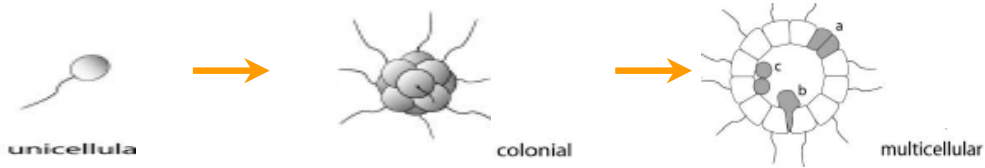


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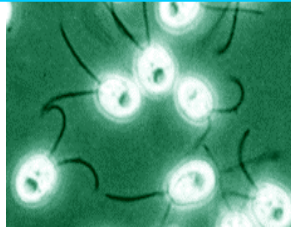


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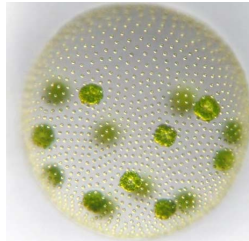
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Chlamydomonas reinhardtii



Volvox carteri

Charophycean algae

Liverworts: *Marchantia polymorpha*

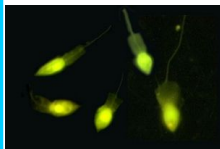
Mosses

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Choanoflagelates

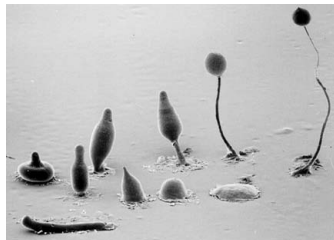


Monosiga brevicollis

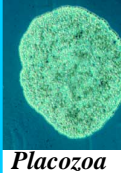


Monosiga ovata

Molecular analysis suggest that animals are more closely related to *Moniga ovata* than to fungi



The social amoeba
Dictyostelium discoideum



Tricoplax adhaerens is thought to be the most anatomically simple multicellular animal.

Placozoa



Sponge

Choanoflagellates closely resemble the choanocytes of sponges and other animals, especially invertebrates

International efforts to trace likely transitions



Cell signaling sits at the top of key developmental regulation

Early evolution of animal cell signaling
and adhesion genes in the sponge *Oscarella carmella*
Nichols, et al. 2006. PNAS, Vol 103, 12451-12456.

Src family of tyrosine kinases is involved in the regulation
of a variety of cell adhesion molecules in *Monosiga ovata*
and in the sponge *Ephydatia fluviatilis*
Segawa, et. al. 2006. PNAS

New miRNAs of the moss *Physcomitrella patens* appear to
play roles in cytokine signaling, which have not been shown
to be regulated by a miRNA in flowering plants.
Talmor-Neiman, et al. 2006. The Plant Journal 47 (1), 25-37.

Implications of the new MicroRNAs reported to be present
in plants and animals
Arteaga-Vazquez et. al. 2006. The Plant Cell.18:3355-3369.

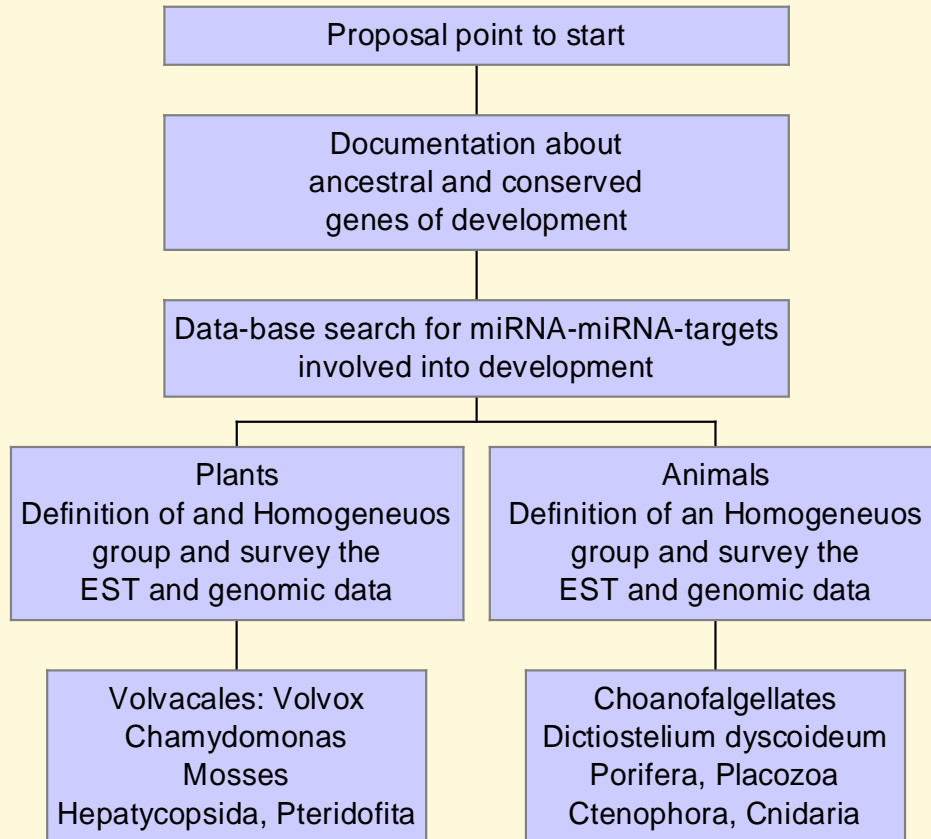


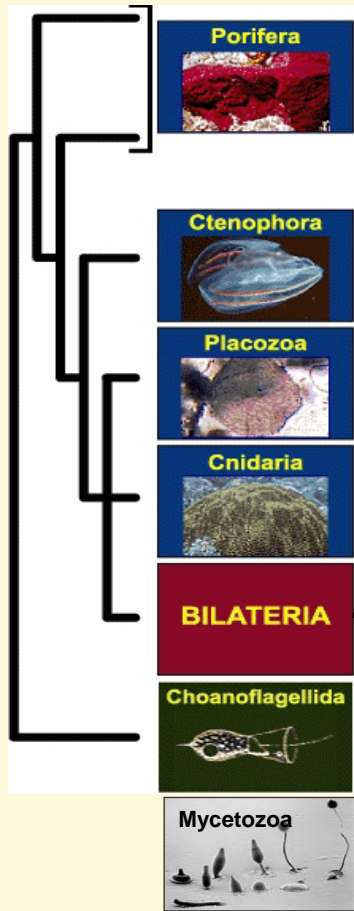


General Aim

Since miRNAs have not found yet in unicellular eukaryotic organism (*Monosiga ovata*, *Chlamydomonas reinhardtii*), colony organisms (*Volvox carteri*, *Dictyostelium discoideum*), simple multicellular animal *Tricoplax adhaerens*, sponge, primitive plants **AND** the importance of miRNAs into the regulation of some pathways of the cell signaling, **THEN** we can hypothesize that the analysis of evolutionary aspects of miRNAs and miRNA-targets constrained to pathways of cell signaling could help us to date back up to miRNA ancient origins.

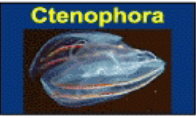






Oscarella carmela: EST: 11176

mRNA isolated from whole tissue of sponge with brooded embryos



Mnemiopsis leidyi: Gastrula stage embryos EST 962. Non genome in process



The simplest known animal: *Tricoplax adhaerens* : 50MB genome in progress



Nematostell vactensis (Anthozoa) 146:976 EST

Hydra manipapillata (Hydrozoa) 174.162 EST



Remain to review



Monosiga ovata: 7391 EST. G. Status in progress

Monosiga bevrucollis: G. Status: Available



Dictyostelium discoideum: 155.032 EST.
Genome sequencing status: draft assembly

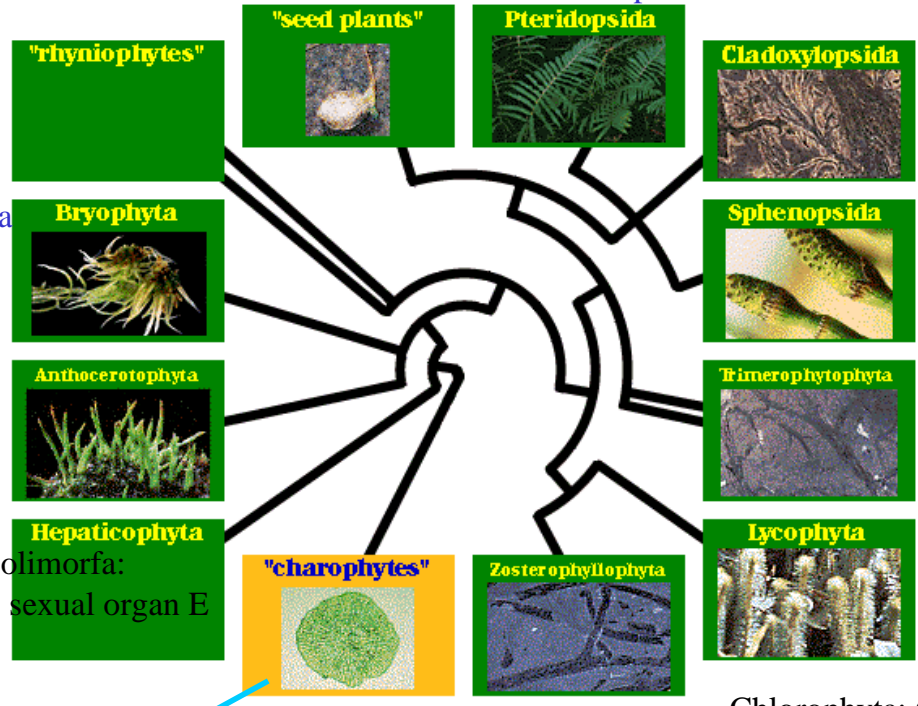




Ceratopteris richardii : 15616 EST

Cycadophyta: 8050 EST: g.p

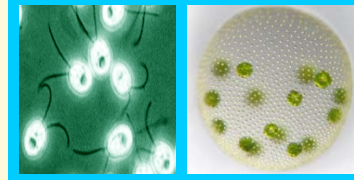
Adiantum capillus 10420 EST



Physcomitrella
patents :
194.822 EST

Marchantia polymorpha:
33.692 EST: sexual organ E

Ulva lianza: 1898
EST: sporulating
thallus



Chlorophyta: Charidomonales
C. renhardtii: genome in
assembly process
Volvox carteri: genome in
progress

Sellaginella
g. p. 2181
EST





TROUBLE, there are new miRNAs predicted
by different levels of detection

Prochnik, et al (2007).
Evidence for a microRNA expansion in bilaterian ancestor.
Dev Genes Evol. 217:73-77.

Three conserved miRNA families in the genome of the sea
anemona *Nematostella vectensis* and no miRNA with confidence
members in the genome of the demosponge *Reniera sp.*
Prochnik, et al (2007). Dev Genes Evol. 217:73-77.

Arteaga-Vázquez, et. al. (2006). A family of MicroRNAs presents
in plants and animals: The Plant Cell. 18:3355-3369

Hertel, et al (2006). The expansion of the
metazoan microRNA repertoire. BMC Genomics. 7:25.





Following, the main problem is in discriminating between real miRNAs and so-called **false positives** and **false negatives**. Therefore, most approaches add to this first step, several filters based on the properties of experimentally documented miRNAs

To implement exhaustive methods to identify miRNA and miRNA targets in the organisms selected. To evaluate *Novo* search too.

To explore some coevolutionary processes among miRNA and their targets

To provide consensus and ancestral sequences of miRNA families genetically associated and of their targets.





To identify some possible relations between miRNA evolution and their regularity function like morphological and developmental innovations as another related functions.

To determine relationships of miRNA/miRNA interactions illustrated by common energetic profile and the patterns observed into the phylogenetic maps of the miRNAs.

To design energetic profile of miRNA and miRNA targets.
To map the biopolymer structures as useful graph theoretical representations.

To establish structural descriptors to correlate known functional properties of miRNA and their structural patterns.





Research activities																		
	First Year						Second Year						Third Year					
	Time bimonthly																	
Activities	1	2	3	4	5	6	1	2	3	4	5	6	1	2	3	4	5	6
Reviewing the genomic data	X	X	X	X														
Searching miRNA and miRNA targets			X	X	X	X												
Phylogenetic analysis							X	X	X									
Mapping biopolymer structures as a graph										X	X	X	X	X				
Structure-function relationships											X	X	X	X				
Bibliography review	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Manuscript													X	X	X	X	X	X

Table 1: Schedule of main research activities



Thank you!



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