Neel Aluru

Postdoctoral Scholar

Biology Department, Woods Hole Oceanographic Institution

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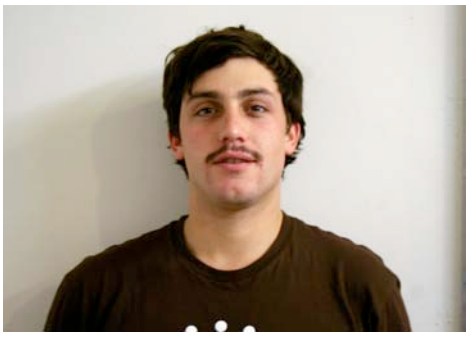
Endocrine regulation of stress response

My research interests are in the field of endocrinology, specifically understanding the mechanisms involved in the endocrine control of adrenal steroidogenesis. Cortisol, the primary glucocorticoid hormone in vertebrates is involved in the regulation of numerous physiological processes including growth and development. The hypothesis of my research is that environmental conditions during early development influences growth in later stages of life and these effects are due to the epigenetic alterations in the gene expression particularly those associated with brain-pituitary-adrenal axis. Using in vitro and in vivo piscine model systems, I am interested in elucidating the early developmental events of cortisol action.

Currently, I am investigating the impact of early exposure to xenobiotic compounds on later stages of life in zebrafish. Microarray results reveal that short term exposure to xenobiotics during early development impacts gene expression patterns in adult life. Majority of the differentially expressed genes are associated with metabolism, immune function and reproduction. Experiments are currently underway to test the hypothesis that epigenetic mechanisms, specifically changes in DNA methylation patterns are responsible for the long term changes in the expression patterns.

Otger Campas
Morphogenesis

During my PhD thesis I studied the generation of cellular movements from a physical point of view. Specifically, I worked on actin-based motility, intracellular transport and cell division. As a postdoc I am working on morphogenesis related questions, using both theoretical and experimental approaches. I first studied the mechanisms that determine cell shape in walled cells, from plants to fungi. The aim of this work is to understand how walled cells regulate and modify their size and shape. Our description provides a framework to understand cell growth and remodeling in plants (pollen tubes, root hairs, etc.), fungi (hyphal growth) and bacteria, and explains the observed variability in cell shapes of several species. At the same time, I got interested in the morphological variability of Darwin's finches beaks. We find that the shapes of the beaks of the 14 species of Darwin's finches are related by simple geometric transformations. By measuring the expression levels of Bmp4 and Calmodulin (the main genes controlling the differences in beak shapes in Darwin's finches) during the early stages of beak development in the different species, we relate the geometric transformations that explain the differences in adult beak morphology to the gene expression levels in the beak primordium. The aim of this work is to relate, at a quantitative level, the geometric transformations that map the beak of one species onto that of another to the underlying developmental processes and, in particular, to the genetics of beak morphogenesis. Finally, I have been developing an experimental set-up to measure physical forces in living embryos and growing tissues.



Social Interactions in Neural Crest Migration

Carmona-Fontaine (or just Carlos)

I am interest in many, maybe too many actually, aspects of biology in general and development in particular. Currently, I am studying the development of the neural crest. I started studying the mechanisms and signals required for the restriction of the area where they are induced. Now, I am particularly interested and dedicated to a later aspect of their development, which is their migration. They are a highly migratory cell population that runs all along the embryo to form structures as distant and different as glands, bones, glias and melanocytes. Narrowing even more what I am doing, I am trying to study the "social interactions" among these migratory cells. More clearly, I am trying to establish how their cell-cell interactions; such as contacts, collisions, attraction and alignment; modify the global behaviour of the migratory stream. The idea would be to understand, in terms of relatively simple interactions, much complex behaviours such as the directional migration of a group.

Sheng-hong Chen (Sheng)

Topic: Approaching DNA damage Checkpoint From Bottom Up and Top Down

Maintenance of genome integrity is essential for cell survival. In response to genotoxic stress, DNA damage checkpoint is activated as the initial signaling event to initiate a variety of cellular responses to repair damaged DNA, arrest cell cycle, and under certain circumstances trigger cell death. It plays a crucial role in the instant DNA damage response for cell viability and in the long-term evolution of organisms.

Bottom Up: While the genetic basis of DNA damage checkpoint has been well characterized in the past decades, the mechanisms of how the DNA damage signal is amplified and transduced downstream remained unclear. I reconstituted the signaling cascade of DNA damage checkpoint *in vitro* with purified proteins. This *in vitro* system was adopted to study the detailed mechanism of signal transduction.

Top down: DNA damage checkpoint is a complex signaling pathway. Mutations in this signaling pathway result in sophisticated phenotypes, including different cancer syndromes. To gain insights into the largely unknown pathways that are targeted by DNA damage checkpoint, we developed a proteomic approach to map kinase-substrate networks by combining quantitative mass spectrometry and a 3-dimensional chromatography. Our results suggested novel processes including epigenetic regulation and chromatin remodeling as targets of DNA damage checkpoint.

Other than biochemistry, I have broad interests in biology. In particular, I am passionate in finding approaches to be able to understand lives in intuitive/holistic ways.

Comparison of acoel and rhabditophoran flatworm stem cell systems: a surprising similarity

Katrien De Mulder

University of Ghent (Belgium) & University of Innsbruck (Austria)

Traditionally, acoel flatworms were seen as an early branching clade within the phylum Platyhelminthes. With the coming age of molecular phylogeny, acoels became separated from other flatworms, although their exact phylogenetic position within the animal kingdom remains elusive. A unique character of flatworms within the Bilateria is the presence of a totipotent stem cell system during adulthood. These stem cells (so called neoblasts) are the only proliferating cells within the organism and form the basis for development, homeostasis and the astonishing regeneration capacity of many flatworm species. However, the question on how acoel and rhabditophoran stem cell systems are related could not be addressed so far since little was known on acoel stem cells and their molecular regulation. During my PhD-studies, we introduced the acoel *Isodiametra pulchra* (Acoela, Acoelomorpha), as potential new model organism, suitable to address developmental questions in this understudied phylum. We established basic molecular tools in order to characterize the stem cell system in detail. By means of BrdU labelling, ultrastructure, Hard-X-ray irradiation, ISH and RNA interference of different stem cell markers such as *piwi, nucleostemin, PCNA, vasa* and *nanos*, we were able to a) follow germline formation and b) to illuminate the morphology, distribution and plasticity of the acoel stem cell system under different developmental conditions. As a comparison, we use *Macrostomum lignano* (Macrostomida, Rhabditophora) as a basal representative for the rhabditophoran flatworms. We identified a potent stem cell system in acoels which shows

astonishing similarities with the so called exceptional stem cell system of platyhelminths regarding distribution, differentiation capacity and function. In addition, we found an extended *piwi*-like gene expression not only in gonadal but also in a subpopulation of somatic stem cells, a second character which share flatworms only with acoels within the Bilateria. We argue that these observations could provide important cues to address the evolution of the stem cell system, which should be taken into account regarding the elucidation of the phylogenetic position of acoels.

Adele M. Doyle
Biomedical Engineering Graduate Student
Georgia Institute of Technology/Emory University

Although stem cells have been proposed for use in clinical therapies, the effects of environmental cues on stem cells remain poorly understood. In the cardiovascular system, these environmental cues include mechanical forces. Cyclic strain due to pulsatile heart contractions and shear stress due to blood flow are both necessary to maintain normal vessel function. Human adult bone marrow-derived mesenchymal stem cells (MSCs) are one potential cell source for vascular cell-based therapies. The focus of my dissertation research is to determine the effects of vascular-relevant applied physical forces on MSCs, in comparison with that of differentiated vascular cells. The central hypothesis is that mechanosensitive cell signaling is conserved between MSCs and differentiated vascular cells. MSCs are compared to aortic smooth muscle cells (SMCs) and endothelial cells (ECs) in the presence of either cyclic strain or steady laminar shear stress, respectively. MSCs undergo cellular rearrangements in a substrate-dependent manner in response to both cyclic strain and laminar shear stress. In a study of the expression levels of 84 signal transduction genes in response to applied strain (10%, 1 Hz for 24 hours), MSCs exhibited a muted strain response compared to SMCs, in terms of both the number and magnitude of gene expression changes. Expression of immune and inflammation-related markers Interleukin 8 (Il8) and Vascular Cell Adhesion Molecule 1 (VCAM1) showed significant ($p \leq 0.5$, $n=3$) changes in both cell types in response to applied strain. These studies identify unique signaling profiles of MSCs compared to SMCs, as well as components of both unique and conserved responses to applied strain. Ongoing studies are comparing the immune and inflammatory response to applied shear stress of MSCs and ECs.

My long-term objective is to bridge biomedical engineering and developmental biology. I am particularly interested in determining the role of mechanical cues during development and design of stem cell-based therapies.

The development of *Platynereis* mesoderm

Antje Fischer

I am investigating the mesoderm- and muscle development of *Platynereis dumerilii* (Annelida), a representative of the Lophotrochozoa. Its development is characterised by spiral cleavage, followed by a lecitotroph trochophora- and metatrophora larval stage. As in all annelids and molluscs, the blastomere 4d gives birth to the trunk mesoderm. Several studies in other model organisms such as *Drosophila* and mouse already revealed genes involved in mesoderm differentiation but only little is known about the mesoderm differentiation in *Platynereis*. My aim is to investigate *Platynereis* mesoderm development on a cellular and molecular level.

On the cellular level, I am investigating the cell lineage of 4d using 4D-microscopy. This is a transmission light microscopy technique using DIC optics. An automated stage allows to record several focal planes over a long time. The first division of 4d leads to the bilaterally arranged sister cells 4d1 and 4d2, which continue to divide in highly synchronised manner and bud off a group of smaller 4d descendants. Up to around 15h hours of development, 4d1 and 4d2 are remarkably bigger than all their offspring. They are the only dividing cells of the mesoderm anlage. At around 15h of development and after six rounds of unequal divisions, they divide almost symmetrically. From then on, their offspring starts to proliferate as well.

On the molecular level, I am examining several transcription factors and differentiation markers involved in mesoderm development using whole mount in situ hybridisation (WMISH) and quantitative PCR. As an example I include in the analyses 3 genes that are known to play a key role in the differentiation of the mesoderm (Twist, Mef2, MyoD) and several genes which are specifically expressed in muscles (Trop, MHC, Mrlc, Melc, Actin), which are known to be one of the main tissues arising from the mesoderm anlage. The onset of Twist and Mef2 coincides with the appearance of cell 4d and its progressive divisions. These findings suggest that one or both genes may be involved in the determination of the mesodermal linage. Morpholino injections will help to clarify the role of Twist and MyoD in *Platynereis*.

e: Claudiu Giurumescu
tion: Postdoctoral fellow, University of California San Diego.
ct: Quantitative analysis of morphogenetic processes at single cell resolution.

I am studying morphogenesis in the model organism *C. elegans* in Prof. Andrew Chisholm's lab at UCSD. Since joining the lab, I have designed a Matlab computer interface for lineaging *C. elegans* embryos, through gastrulation and part of their morphogenesis using histone-GFP nuclear markers. Currently and in the future I plan to use this platform for constructing 4D atlases of morphogenesis in *C. elegans* mutants that display abnormal body morphogenesis by following their embryonic development. In particular I am looking at VAB-1 and TOL-1 mutants. VAB-1 is the only Eph receptor in *C. elegans*, and while we know that mutations in the receptor lead to variable abnormal morphology without change in the cell lineage, little is know about the cellular basis of these abnormalities. Hence, I plan on developing reporters for the VAB-1 receptor and its known ligands, the ephrins EFN-1-4. Using dual color histone-GFP nuclear marker and mCherry reporter we should be able to discover the cells in which VAB-1 acts. Since some of VAB-1 mutant embryos arrest at a stage synchronous with the formation of worm's ventral cord, it will also be interesting in investigating the role of Eph receptor in the processes guiding the intercalation of bilateral neuroblasts. TOL-1 is the sole Toll-like receptor in *C. elegans*. Null mutants of *tol-1* show more than 90% embryonic lethality, but those embryos that develop do not show adult morphology defects. I plan to investigate the role of TOL-1 in embryonic morphogenesis by looking at changes in the cell lineage and cell-cell nearest-neighbor relationships. I am also planning on using targeted cell ablation to further understand the cellular basis of these morphogenetic defects.

Transcriptome analysis of development in the coral *Acropora millepora*.

Lauretta Grasso

Natural and anthropogenic effects are taking their toll on coral reefs, some in ways affecting the developmental cycle of corals. In order to truly understand their impacts, a more thorough understanding of the molecular basis of development in corals is required. Furthermore, my study species, *Acropora millepora*, a common reef building coral in the inshore areas of the Great Barrier Reef, has in the last 10 or so years been established as a model organism for evo-devo studies. In light of this, my PhD involved two main experiments studying the molecular control of development in the coral *A. millepora* on a genomic scale. Firstly, cDNA microarrays for *A. millepora* were used to assay for gene expression changes throughout the development of this organism by comparing transcript abundance in four disparate developmental stages. From these, candidate genes for involvement in settlement and metamorphosis, calcification and symbiont recognition, some homologous to known proteins and some “coral specific”, were isolated and further characterized by in situ hybridization. A second microarray experiment focused on discovering the changes in gene expression underlying settlement and metamorphosis. In this experiment microarrays were used to compare transcript levels in competent presettlement larvae with those in larvae treated with stimuli known to induce settlement and/or metamorphosis in this species. Chips and an ethanolic extract of a crustose coralline algae species, and the neuropeptide LWamide were used as stimuli on replicated sets of competent larvae, which were then sampled at 0.5, 4, and 12 hours post-induction. A set of potential key settlement/metamorphosis genes could be identified. By correlating changes in gene expression to changes in morphology at different times under different treatments it was possible to sort genes into "early response" and "late response" groups, each with a characteristic expression pattern.

Alysha Heimberg

Evolution of Animal microRNAs and Morphological Novelty

I am broadly interested in the origin and evolution of morphological traits. In lab I have been examining this question specifically in the context of how microRNA genes may have changed the regulatory landscape of animal genomes throughout evolution to allow for origin or success of morphological changes. I'm interested in microRNA gene regulation because there is a strong correlation between microRNA acquisition and animal complexity. I have been constructing and sequencing microRNA libraries and studying the comparative biology of animals from many different phyla, focusing on select basal metazoans (sponges and cnidarians) and chordates (amphioxus, hagfish, and lamprey).

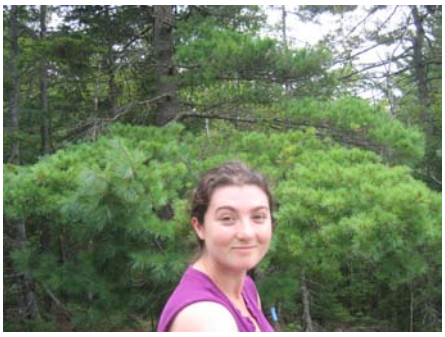
Francie Hyndman

Lower jaw development is a complex process orchestrated by signaling cascades that are regulated temporspatially and are constantly refined through permissive and inhibitory signals. We have previously shown that endothelin-A receptor (Ednra) signaling is crucial for establishing the identity of cranial neural crest cells (NCCs) in the mandibular pharyngeal arch through a mechanism that involves *Dlx5* and *Dlx6*. *Dlx5/6* in turn induce expression of the gene encoding the basic helix-loop-helix transcription factor Hand2. While this pathway places *Hand2* at the center of a complex signaling cascade, little is known about the function of Hand2 in mammalian facial development because *Hand2*$^{-/-}$ embryos die by embryonic day (E) 10.5 from vascular failure.

To circumvent this lethality, we created a conditional targeted *Hand2* mouse line using a Cre-*lox*P approach. Using the *Wnt1-Cre* mouse line, we selectively deleted *Hand2* within all NCCs. We find that Hand2 conditional knockout mice exhibit facial defects that include mandibular hypoplasia and absence of the tongue (aglossia). The aglossia is preceded by aberrant maintenance of *Dlx5/6* expression in the disto-oral mandibular arch mesenchyme. In vitro studies show that Hand2 represses the *Dlx5/6* pharyngeal arch-specific enhancer. Together, these data suggest that Hand2 normally ensures normal tongue development by repressing *Dlx5/6* expression within the disto-oral mandibular arch. In the absence of Hand2, *Dlx5/6* expression is maintained and ectopically activates an osteogenic program at the expense of a tongue development program.

Erin Kaltenbrun

Cardiogenesis occurs through series of coordinated events in the developing embryo that give rise to a mature heart. These events include specification of cells into the cardiac lineage, migration, differentiation, and morphogenesis. The Notch pathway is involved in many of these processes, including cardiomyocyte differentiation, atrioventricular canal development, valve development, and ventricular trabeculation. While it is well documented that Notch acts as a potent inhibitor of cardiomyocyte differentiation, it is not clear whether Notch directly regulates terminal differentiation, or whether the failure of cardiomyocytes to differentiate in the presence of Notch signaling is a secondary consequence of a role of Notch in regulating cardiac progenitor proliferation. In order to investigate the role of Notch in regulating the relationship between proliferation and differentiation of cardiomyocytes, we are developing a novel approach to isolate cardiac progenitors from mouse embryonic tissue. This method employs site-specific biotinylation of all *Nkx2.5*-expressing cells and subsequent isolation of biotinylated Nkx2.5^{+} cells using streptravidin beads. This method will allow for the isolation of small populations of cardiac progenitors (400-600 cells/E8.5 embryo) from wild-type and mutant embryos versus a traditional FACS. Enriched populations of cardiac progenitors will then be used to assess the effects of Notch manipulation on the proliferation and cell cycle progression of cardiac progenitor cells prior to the onset of terminal differentiation.



Deirdre Lyons

Evolution of the spiral cleavage program

The early development of many metazoans proceeds via highly stereotyped cleavage patterns that asymmetrically segregate fate determinants and are critical for establishing the axes of the adult body plan. Spiral cleavage is characteristic of many lophotrochozoan phyla with disparate morphologies, including annelids, molluscs, nemerteans and polyclad flatworms. Comparative analysis of spiralian development offers unparalleled opportunities to understand how the evolution of divergent body plans is achieved by innovations within a conserved embryological framework. For example, although the spiral cleavage program is remarkably conserved overall, species-specific variations in cell division asymmetry, spindle orientation, cell cycle duration and cell fate determination exist, suggesting that such changes are the basis for morphological divergence. However, the mechanisms controlling the spiral cleavage program remain poorly understood.

As a graduate student, I used the leech *Helobdella* to examine the cell biological mechanisms controlling the asymmetry and chirality of the CD cell division at second cleavage, a key step in breaking bilateral symmetry. I showed that the unequal CD cleavage is controlled by the rightward displacement of a symmetric mitotic apparatus in an actomyosin-dependent process. Our data also revealed that within the monophyletic clitellate annelids their homologous spiral cleavage pattern has diverged significantly at the level of cell biological mechanisms. This combination of operational conservation and mechanistic divergence begins to explain how the spiral cleavage program has remained so refractory to change while, paradoxically, accommodating numerous modifications throughout evolution.

Establishment of polar identities and germ layers during planarian

development

Chema Martín-Durán
Dpt. of Genetics. University of Barcelona

My work is focused on the study of planarian embryology by means of molecular markers and the development of novel techniques, using as a model the sexual species *Schmidtea polychroa*. Planarians lay polyembryonic eggs packaged inside a spherical hard and dark egg capsule or cocoon. Planarian embryos are characterized by ectolecithy, or the storage of yolk content outside the embryo, in specialized cells called yolk cells. This trait constrains the whole process, so planarian embryos quickly and early in their development make transient structures (an embryonic pharynx, gut and epidermis) to swallow the yolk content and keep it into them for the rest of the embryology. These organs are later on replaced by the definitive tissues, and it is during this replacement when the final morphology of a planarian arises.

As a first step to study the embryology of these animals at the molecular level, I have been looking into the establishment of polar identities and the acquisition of the definitive shape during development. For this purpose, we cloned and studied the expression during development of ßcatenin and BMP, genes known to play a crucial role in specifying posterior and dorsal identities in planarians, respectively. Our data show that a primary anterior-posterior axis is established early in development, appearing the dorso-ventral one relatively late, when the definitive structures start to be specified. Furthermore, the transitory embryonic organs of the early stages of development seem to be arranged in the early spherical embryo following this AP axis.

By studying the expression of mesodermal, endodermal and ectodermal genes, we have observed that there is no clear segregation of germ layers during the first stages of development. Blastomeres committed to the basic cell fates are placed instead in a thin layer, the germ band. After the embryo ingests the yolk content, these blastomeres proliferate and give rise to the final mesodermal, endodermal and ectodermal tissues. In parallel, I have been developing new techniques to get access to the living embryos inside the egg capsule. By means of laser microdissection techniques, we have managed to perforate the tough eggshell and microinject exogenous material into the embryos without completely disturbing their development.

This work, in sum, demonstrates that despite of the idiosyncrasy of planarian embryology, basic and common developmental traits to all metazoans are still discernible during its development.

Lara Marxreiter

Neural tube defects (NTDs) are one of the most common birth defects afflicting 1 in 1000 to as high as 1 in 100 live births. Both genetic and environmental factors have been implicated in the incorrect or incomplete closure of the neural tube. In order to elucidate the genetic factors, our lab identified a novel HECT domain E3 ubiquitin ligase (Hectd1) required for neural tube closure. E3 ubiquitin ligases determine the fates of proteins by attaching a ubiquitin peptide to a target protein, resulting in its degradation or functional modification. The key to understanding the role of Hectd1 in neural tube closure is to determine its protein targets and define the pathways it regulates. Since Hectd1 ligases directly bind to substrates, a yeast-two hybrid screen was performed to identify binding partners. From this screen, twenty-one candidate proteins were identified which regulate many different cellular processes such as cytoskeletal organization, transcription, signal transduction, and chromatin remodeling. Our current research is validating whether these candidates bind Hectd1 and are substrates of this E3 ligase. The ultimate goal of these studies is to determine how the loss of Hectd1 dependent ubiquitination of these substrates results in NTDs.

Vincent Pasque

Investigating nuclear reprogramming by nuclear transfer to Xenopus eggs and oocytes

Reprogramming somatic cells into stem cell-like cells holds great promise for regenerative medicine and the generation of patient-specific stem cells. However, the molecular mechanisms by which the nucleus of a differentiated cell can be reprogrammed to an embryonic stem cell-like state are poorly understood. While several approaches exist to induce nuclear reprogramming, I am using somatic cell nuclear transfer to Xenopus oocytes or eggs.

No cell division occurs in the oocyte system, when multiple somatic cell nuclei are transplanted into the nucleus of the meiotic prophase oocyte. Following transfer, nuclei are directly induced to express previously silenced stem cell genes within a few hours or days. Importantly, transcriptional reactivation occurs in the absence of DNA synthesis, and no new cell types are created. Using this system, I am particularly interested in a process that is resistant to nuclear reprogramming, that of the mammalian inactive X chromosome. I have set out to analyse changes in chromatin structure, transcription and *Xist* RNA localisation after nuclear transfer. I am using a combination of mouse genetics and nuclear transfer to test how individual silencing mechanisms may limit X chromosome reactivation.

In addition, nuclear transfer embryos can be obtained when single somatic cell nuclei are transplanted into enucleated eggs. However, most nuclear transfer embryos obtained by this route show developmental abnormalities, while a small proportion successfully develop into fertile adults. This low success rate in nuclear transfer experiments is thought to be due, in part, to the incomplete erasure of epigenetic marks. I am interested in how DNA methylation may regulate memory of transcriptional states in nuclear transfer embryos, which has not been analysed in great detail in the frog. A particular focus is put on the mesodermal inducer Xbra, whose expression is thought to be dependent on promoter DNA demethylation. Using donor cell nuclei with normal or reduced DNA methylation levels, I am testing how DNA methylation influences nuclear transfer efficiency as well as transcriptional memory in nuclear transfer embryos.

Malea Murphy

University of Utah

Vertebrate muscle has a remarkable capacity for regeneration. Regeneration is largely mediated by satellite cells, which must become activated, proliferate, and differentiate to repair damaged myofibers. Interactions with the surrounding muscle connective tissue are likely to be important for muscle regeneration. The muscle connective tissue is composed largely of extracellular matrix (ECM) embedded within which are a small number of fibroblasts that presumably produce the ECM. This connective tissue enwraps muscle, maintaining muscle structural integrity and transmitting muscle contractile force to adjoining tendon and bone. During muscle regeneration there is an increase in connective tissue ECM, termed fibrosis, which maintains the structure of the damaged muscle and may be an important source of signals regulating satellite cells. However, excessive connective tissue ECM can inhibit muscle regeneration. Thus, connective tissue must be precisely regulated for proper muscle regeneration. Therefore interactions between connective tissue fibroblasts, satellite cells, and fibrosis are likely critical for normal regeneration. To characterize the interactions between muscle and its connective tissue during muscle regeneration, we have determined the temporal and spatial relationship between satellite cells, connective tissue fibroblasts, myofiber regeneration, and fibrosis after muscle injury. We find that satellite cells and connective tissue fibroblasts expand in concert in regions that are enriched in regenerating myofibers and connective tissue fibrosis.

Proximodistal axis of the limb bud: a meeting place for RA, FGFs and adhesion properties

Name: Alberto Roselló

My first project deals with the role of retinoic acid (RA) and Fibroblasts growth factors (FGFs) in the specification of proximodistal (PD) fates in the chicken limb bud. We have evidence indicating that PD limb fates are not autonomously specified, as they depend on the amount of RA diffusing from the flank and on FGF signaling from the AER. This was previously suggested some years ago, but we have new direct evidences to fine-tune the model.

The second project consists in overexpressing the proximally-restricted transcription factor *Meis2* (a likely target of RA) in a postero-distal domain of the mouse limb, to see how it affects normal development. We have found that MEIS2 confers different adhesion properties to the cells that express it, as compared to the surrounding non-expressing cells. By means of a microarray approach we are studying which are the surface molecules involved in this change of adhesive properties. Finding them would be very interesting, as it would shed light on the question of how the different PD segments are generated from a homogenous population of cells.

In the third project we are trying to trace the lineage of cells that at a particular time point expressed genes relevant for PD development (namely *Meis1*, *Hoxa11* and *Hoxa13*). For this to be done, we are generating three different Knock-in mice in which one of the alleles of one of the three relevant genes is substituted by a cassette coding for an inducible Cre recombinase. This will allow us to trace at a clonal level the lineage of the cells that express those genes, hopefully unraveling the relationship between them and the specification of PD fates.

Prashant Sharma

I am broadly interested in macroevolution, biogeography, speciation, and empirical studies of phylogeny. My dissertation project addresses the biogeography of Southeast Asia and the Southwest Pacific, and the evolution of arthropods on the numerous islands and archipelagoes in this region. This inquiry is driven by questions of how species have colonized distant islands and how the diverse geological histories of the islands in this region have affected the evolution of these lineages. I address these questions through an increasingly powerful model system for biogeographical studies, Opiliones. Opiliones is an order of small arachnids commonly known as daddy-long-legs or harvestmen. Though superficially resembling spiders (Araneae), they are more closely related to scorpions. I am presently working on the phylogeny of one particularly curious family, Zalmoxidae, that occurs throughout Southeast Asia and the Southwest Pacific, as well as on the broader phylogenetic resolution of Laniatores, the suborder that includes Zalmoxidae.

Ashley Siegel (University of Missouri)

Intrinsic and extrinsic factors affecting satellite cell migration

Satellite cells are adult stem cells that are present in all skeletal muscle tissue, and are responsible for repair, regeneration, and replacement of all skeletal muscle over an entire lifetime. They are competent to respond to either a systemic insult or an acute trauma. When muscle is injured, satellite cells will leave the quiescent state that they are normally held in, proliferate extensively to form a population of differentiation-competent myoblasts, migrate to the site(s) where repair is needed, and then differentiate and fuse to precisely and efficiently restore muscle patterning and function. Our lab focuses on the molecular mechanisms by which adult muscle stem cells (satellite cells) receive, integrate, and respond to signals from their local environment to produce timely and appropriate muscle regeneration. My interest is in the migratory abilities of satellite cells. I believe that satellite cells are not only capable of migrating but that it is necessary for correct regeneration and growth of skeletal muscle.

My aim is to begin elucidating the intrinsic and extrinsic factors that control the directed migration of satellite cells in vivo. This research is not only critical to improving therapy for disease such as DMD but will also bring light to some of the conserved migratory pathways of developing cells and adult stem cells.

Ajay Thomas

The effect of folic acid supplementation on neural tube defects and gene expression.

In 1996 the FDA instated regulations requiring the addition of folic acid to enriched breads, cereals, flours and other grain products. The ruling was based on previous research that found a decrease in occurrence and recurrence of neural tube defects after folic acid supplementation. Folic acid is an important vitamin that is integral to three main biosynthetic pathways: single carbon transfer reactions (methylation), thymidylate synthesis, and purine synthesis. Some tout folic acid as a panacea and have linked folic acid fortification to decreased rates of congenital heart defects, stroke, and cancers among other diseases. Even with these favorable connections to folic acid supplementation, much controversy still surrounds the issue. Recent research has shown that folic acid supplementation may be harmful in certain situations. Previous studies have shown a genetic variation in folate metabolism which may cause variability in responses to folic acid supplementation. While folic acid supplementation may yield positive outcomes for some, in others supplementation may come as a detriment. The underlying mechanisms of folate metabolism are still unclear. We plan to use various mouse models of neural tube defects to study the yet to be elucidated mechanisms of folate metabolism. Mainly, these various genetic approaches may point to genetically-based variability in response to folic acid response. Recent studies have shown a link between folic acid supplementation and perturbation of DNA methylation. The full impact of this change in DNA methylation is not yet known. In addition to studying genetic variability of neural tube defects with folic acid supplementation, we plan to study the implications of folic acid supplementation on DNA methylation and gene expression.

Frank Tulenko

Biology Dept.
Wesleyan University
Middletown, CT 06457

Body Wall Formation in Lamprey: Insights from the Ontogeny of an Agnathan

I am interested in vertebrate evolution, and how changes in developmental programs underlie morphologic innovation. Patterning of the musculoskeletal system from embryonic mesoderm has diverged considerably over more than 400 million years of vertebrate evolution, resulting in extraordinary morphological variation across taxonomic groups. In vertebrates, skeletal muscle derives from somitic mesoderm. Whereas most axial musculature is primaxial, forming from somitic cells that differentiate in a somitic environment, muscles of the limbs, diaphragm, and abdominal body wall are abaxial and derive from somitic migratory cells that enter the lateral plate. The lateral somitic frontier (LSF) marks the interface between the primaxial and abaxial domains. Although the LSF has been mapped in mouse and chick, its position in anamniotes is unknown. Lamprey lack jaws and paired fins, and diverged from other vertebrates prior to the radiation of gnathostomes. Thus, lamprey are a key model system for gaining insight into both the ontogeny of basal vertebrates and the key evolutionary innovations of gnathostomes. Thus far, I have performed experiments using DiI to label presumptive lateral plate cells in the Japanese River Lamprey (*Lethenteron japonicum*) to determine the fate of these cells in an agnathan vertebrate. Preliminary results indicate that DiI-labeled cells contribute to the lining of the body coelom and contact the ventral edge of the growing myotome, but are never found superficial to the myotome or mixed with myofibers. These data suggest that the lamprey myotome is entirely primaxial. Furthermore, as the myotome grows ventrally during body wall closure it displaces the lateral mesoderm, restricting these cells to the inner ventral body wall. I hypothesize that the primitive vertebrate trunk was primaxial, and changes in the behavior of cells at the LSF were important in expansion of the abaxial domain and the origin of paired appendages. In the future, I hope to determine if homologous marker genes are expressed in both lamprey and gnathostome lateral plate. Additionally, I would like to elucidate the mechanistic underpinnings of the differential tissue movements described above.

Name: Alex Vasilyev

Position: Research Fellow, MGH

My main interest is kidney morphogenesis. As a research fellow in Iain Drummond's lab I recently characterized a novel process of collective epithelial cell migration in a developing zebrafish kidney. In this process, polarized kidney epithelial cells migrate towards the glomerulus, apparently in response to luminal fluid flow (moving against the flow). This epithelial migration determines the final positions of kidney segment boundaries and leads to the proximal nephron convolution. I am currently working to characterize this process in cellular and molecular detail and to further explore the role of epithelial migration in nephron development and regeneration.

Naveen Wijesena

Graduate Student

Department of Biology

University of Miami

Research Interests

I am broadly interested in evolutionary biology and how biological and environmental factors affect evolution. At present my focus is on evolutionary developmental biology and my dissertation research is aimed at investigating the role of Wnt signaling on the evolution of embryonic polarity in metazoan embryos. I'm looking at how different components of the Wnt/PCP pathway regulate embryonic polarity and cell fate specification and morphogenesis during gastrulation in the developing embryo of the anthozoan cnidarian *Nematostella vectensis*. Since cnidarians are considered to be the sister group for all bilaterally symmetrical animals, *N. vectensis* is an ideal model organism for studies aimed at gaining insight into the evolution of embryonic polarity in the metazoan lineage.