ECOLOGICAL IMPLICATIONS OF CROSS-GENERATIONAL EFFECTS

The 15th Sede Boqer Symposium in Memory of Merav Ziv

22 May, 2014

George Evens Family Auditorium
The Jacob Blaustein Institutes for Desert Research
Ben-Gurion University of the Negev, Sede Boqer Campus
Midreshet Ben-Gurion

אוניברסיטת בן-גוריון בנגב
Ben-Gurion University of the Negev

Jacob Blaustein Center for Scientific Cooperation

The Swiss Institute for Dryland Environmental and Energy Research

Mitrani Department of Desert Ecology

The Zoological Society of Israel

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Program

09:30	*Reception & refreshments*
09:45	*Memories of Merav & Ecology Student Awards*
10:00-10:45	*Keynote*- **Eva Jablonka** (Tel Aviv University), Evolutionary epigenetics.
10:45-11:30	*Keynote*- **Koen Verhoeven** (Netherlands Institute of Ecology), Ecological epigenetics: exploring the causes and consequences of natural epigenetic variation.
11:30-11:45	*Refreshments*
11:45-12:15	**Lior David** (Hebrew University), Roles of genetic and epigenetic processes in evolving new gene regulation in yeast
12:15-12:45	**Michal Horowitz** (Hebrew University), Heat acclimation plasticity: Are epigenetic processes involved?
12:45-13:00	*Discussion*
13:00-14:10	*Lunch*
14:10-14:40	**Roei Shaham** (Haifa University), Parental epigenetic effects: Genome methylation patterns across castes and developmental stages in a parasitoid wasp
14:40-15:20	**Simone Immler** (Uppsala University), The role of sperm-mediated transgenerational epigenetic effects in the zebrafish
15:20-15:50	**Oded Rechavi** (Tel Aviv University), Transgenerational inheritance of small RNAs in *C. elegans*
15:50-16:00	*Refreshments*
16:00-16:30	**Nir Ohad** (Tel Aviv University), The role of epigenetic regulation in land plants reproduction and phase transition
16:30-17:00	**Gideon Grafi** (Ben-Gurion University), Reduced epigenetic constraints in the Zygophyllaceae family
17:00-	*Discussion & summing up*

Evolutionary epigenetics

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There is general acceptance today that epigenetic mechanisms play an important role in both development and heredity, underlying many modes of transmission between generations and accounting for many epidemiological and ecological observations. The role of epigenetic inheritance in evolution, is, however still debated. In this lecture I examine observations and models showing (i) the effects of ontogenetic epigenetic inheritance during development on evolutionary change; (ii) the micro-evolutionary (population level) effects of trans-generational epigenetic inheritance; (iii) the effects of epigenetic inheritance on macro-evolutionary changes. I highlight the role of epigenetic mechanisms in the phenotypic, adaptive adjustments of organisms to novel and often stressful conditions, and suggest that that epigenetic inheritance may play an important role in speciation. I conclude that evolutionary epigenetics has come of age and must become an integral and normal part of the study of evolutionary change.

Ecological epigenetics: Exploring the causes and consequences of natural epigenetic variation

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Epigenetic mechanisms such as DNA methylation can stably regulate gene and transposon activity. Epigenetic patterns are sensitive to environmental inputs, and epigenetic mechanisms can therefore play a role in how a genome is translated into a transcriptome that is tailored to local environments. With growing evidence that some of the epigenetic code is heritable between generations there is increasing awareness that epigenetic variation might play a role in short-term adaptation of populations. Here I will give an overview of recent developments in the field of ecological epigenetics, which aims to investigate the epigenetic contribution to adaptation, and I will illustrate this with examples from our work in plant lineages that lack genetic variation, apomictic dandelions and inbred Arabidopsis. Lacking genetic variation, these study systems are well-suited for exposing the effects of epigenetic inheritance that is not confounded with genetic differences. I will discuss two different aspects of heritable epigenetic variation: epigenetics as an underlying mechanism of transgenerational phenotypic plasticity (or transgenerational effects), and stable but essentially random epigenetic variation that may be shaped by selection. With respect to the first, we explore transgenerational effects of biotic and abiotic stress exposure at the DNA methylation, transcriptome, metabolome and trait levels. With respect to the second, we explore patterns of standing heritable epigenetic variation in natural populations and between clone members within widespread apomictic dandelion genotypes. These studies can yield first insights into the role the epigenetic variation plays in the wild.

Roles of genetic and epigenetic processes in evolving new gene regulation in yeast

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The basic evolutionary process provides a way, and maybe the only long-term way, to coordinate between environmental conditions and the organisms living under them. Therefore, adaptation is a way allowing the organism to acquire changes in the face of environmental challenges and to inherit these changes to its decedents. Evolutionary studies demonstrated that mutations happen rarely, randomly in the genome and apart from the environment in which they confer a phenotypic advantage. Thus, the established way for adaptation is selection of advantageous individuals and consequently of rare advantageous mutations. However, this evolutionary strategy might not suffice for adaptation to unforeseen challenges. We have established an experimental system in the lab to study the process of yeast adaptation when confronted with a novel regulatory challenge. We placed *HIS3,* an essential gene for histidine biosynthesis, exclusively under the promoter of *GAL1,* a gene belonging to the GAL system, which is necessary only for utilization of galactose as a carbon source. The GAL system repression in glucose confronted these rewired cells with a severe regulatory challenge. We have analyzed numerous adaptation experiments using different techniques and found out several important findings:

1. An average of 50% of the cells adapted to grow on glucose medium. Rather than finding rare advantageous variants adapting, many cells have developed new ways to regulate *HIS3,* ways that were successfully inherited to following generations.
2. This high proportion of adapted cells was not reached by a strong selection of few rare variants that existed in the population prior to the environmental challenge. Instead, the challenging environment induced the inherited adaptation independently in many cells.
3. Underlying this adaptation was reorganization of a new gene regulation network. Different combinations of genetic and epigenetic changes facilitated multiple ways of network reorganization leading to adaptation of that many cells.

Taken together, using our unique experimental system we were able to connect the evolutionary process of adaptation with underlying genetic changes, but more importantly with epigenetic changes. Conceptually, epigenetics mediates environmental and short-term physiological change. Here we extend the concept to include epigenetics as a mediator of adaptive changes including mutations, which are relevant to the longer-term evolutionary development of organisms.

Heat acclimation plasticity: Are epigenetic processes involved?

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Adaptation to environmental stress is an evolutionary conserved feature, allowing enhanced tolerance, cross tolerance and adaptive memory to adverse environments, while employing powerful physiologically-controlled and metabolically coping tools when stressed. To achieve these fast responding features, the organism undergoes long-term adaptive process involving temporally changing short and long-term molecular and cellular programs. Using the heat acclimated cardio-phenotype in rats and Heat Shock Proteins (HSP) as a model system, in this presentation these programs are discussed. The onset of acclimation is of transient nature. Up/down-regulated genes linked to maintenance of DNA integrity, decreased histone H1 transcript level and increased miRNAs emphasize the strain at the onset of acclimation phase. This phase is considered as the molecular 'on-switch' of acclimation. Histone H3 phosphorylation at this acclimation phase, leading to constitutive histone H4 acetylation and HSF1 binding at the HSPs 70 and 90 genes during the entire session of the acclimation regimen is only one among the mechanisms of enhanced cytoprotection. The latter cascade leads to augmented HSPs reserves and in turn to enhanced thermotolerance and cytoprotection. Testing the HSPs system in evolutionary adapted diurnal and nocturnal desert rodents while heat acclimation, we demonstrated similar HSP reserve augmentation, suggesting that at least partially, acclimation recapitulates evolutionary adaptation. Proteomic analyses revealed that the diurnal desert rodents (*Acomys russatus, Psammomys obesus*) have less HSP70 isoforms than nocturnal congeners (*A. cahirinus, Merioness crassus*) thereby diminishing diurnals cytoprotective flexibility. The HSF1-HSP interaction to affect acclimation plasticity is discussed.

Parental epigenetic effects: Genome methylation patterns across castes and developmental stages in a parasitoid wasp

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Trans-generational environmental influences (also known as parental effects) play a crucial role in determination of offspring phenotype. In vertebrates, these influences often involve modifications of the offspring genome by methylation of DNA segments that affects expression of genes, via epigenetic control. Modification of methylation patterns also mediates caste determination and task allocation in eusocial insects, such as honeybees and ants. However, the influences of parental effects on methylation patterns in insects are yet unknown. In particular, the persistence of these patterns during holometabolean development has not yet been studied. We aim to further understand these methylation dynamics, using the polyembryonic parasitoid wasp *Copidosoma koehleri*, which also features a unique, simple caste system, as an experimental model.

We exposed individuals to either high or low rearing density as larvae, and compared methylation patterns in their offspring at three developmental stages (larvae, pupae and adults) using the methylation sensitive amplified fragments length polymorphism (MS-AFLP) method. In addition we exploited the caste system of this wasp to test for differences in methylation patterns between its reproductive and soldier larvae.

Preliminary results on methylation patterns in reproductive and soldier larvae, suggest that differential methylation sites exist in both castes. Further work regarding the methylation dynamics at different developmental stages is still in progress.

The role of sperm-mediated transgenerational epigenetic effects in the zebrafish

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The existence of transgenerational non-genetic inheritance is increasingly recognized to play a major role in evolutionary processes and inheritance. While the causes and consequences of epigenetic effects transmitted from the mother to the offspring have received ample attention, much less is known about how variation in the condition of the father affects the offspring. Our research investigates the potential role of paternally inherited epigenetic effects in the zebrafish *Danio rerio*. We manipulate the sperm competition environment of male zebrafish and monitor the effects of this manipulation of the paternal environment on sperm motility and velocity but also on the performance and fitness of the resulting offspring. In addition, we are investigating the underlying molecular mechanisms in the sperm and monitor effects on gene expression in the offspring. I present an overview of the potential role and underlying mechanisms of paternal epigenetic effects in the zebrafish and present the results from our recent experiments. Our results provide striking evidence for short-term paternal effects and the possible fitness consequences of sperm-mediated non-genetic factors not only for the male and the resulting offspring but also for the female.

Transgenerational inheritance of small RNAs in *C. elegans*

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The inheritance of acquired characteristics is a topic of long-standing interest and controversy. While some of the classic Lamarckian ideas have been dismissed, more recent studies suggest that certain traits acquired by an animal during its lifetime may be transmitted to next generations. *C. elegans* inherits acquired antiviral and transposon resistance (in a "Lamarckian" fashion) through transgenerational transmission of small RNAs, which mediate RNA interference. Inherited small RNAs, which protect the worm, can be passed down to many ensuing generations in a non-Mendelian manner, and "vaccinate" RNAi-deficient progeny. Most genes are regulated by different endogenous regulatory small RNA species, and therefore small RNA inheritance might affect the inheritance of many traits. Our recent efforts suggest that inherited small RNAs may indeed reflect the ancestral environment, and possibly prepare the progeny for relevant hardships.

The role of epigenetic regulation in land plants reproduction and phase transition

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Land plants are characterized by alternation of generations, in which the diploid multicellular sporophyte develops after fertilization and the haploid gametophyte emerges following meiosis. A key component regulating this cycle is the Polycomb group complex (PcG) which catalyzes histone H3K27 methylation, facilitating epigenetic control of gene expression profiles.

Using the moss *Physcomitrella patens* as a model system of early terrestrial plants, we study the function of the PcG genes. We found that FIE PcG protein (PpFIE) accumulates in haploid meristematic cells and cells which undergo fate transition during dedifferentiation programs in the gametophyte. In the absence of PpFIE, apical stem cells over-proliferate and are unable to develop leafy gametophytes thus reaching the reproductive phase. However PpFIE mutants develop sporophytic-like structures expressing gene markers unique to this phase. The PpFIE aberrant mutant phenotype can be partially rescued by the *Arabidopsis thaliana FIE* gene, representative of angiosperms, thus illustrating functional conservation of the protein throughout plant evolution. Previously we have shown that in *Arabidopsis*, DNA methylation mediated by the methyltransferase1 (MET1) take also part in the regulation of gene expression during the reproductive cycle. Although the role of DNA methylation has been intensively studied in flowering plants, little is known about the evolution of this mechanism. To understand the biological role of DNA methylation in early terrestrial plants we identified single homologous of the *Arabidopsis* methyltransferases MET1 and CMT3 in *Physcomitrella patens* and studied their function. Mutants lacking *PpCMT* gene or *PpMET* display dramatic inhibition of growth during the gametophytic phase and inability to reproduce respectively. Employing bisulfite DNA sequencing, we were able to determine the biochemical function of both methyltransferases in-vivo. Based on these results the regulatory role of DNA methylation and H3K27 methylation during moss development will be discussed.

Reduced epigenetic constraints in the Zygophyllaceae family

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Zygophyllum dumosum Boiss. is a perennial Saharo-Arabian phytogeographical element and a dominant shrub on the rocky limestone southeast-facing slopes of the Negev desert. Being resistant to extreme perennial drought, *Z. dumosum* appears to provide a suitable plant for studying epigenetic mechanisms associated with drought tolerance in natural habitats. We found that the transition from the wet to the dry season was accompanied by a significant decrease in nuclear size associated with posttranslational modifications of histone H3 N-terminal tail. Dimethylation of H3 at lysine 4 (H3K4) – a modification associated with active gene expression – was found to be high during the wet season but gradually diminished on progression to the dry season. Unexpectedly, in contrast to other desert plants, H3K9 dimethylation and trimethylation could not be detected in *Z. dumosum;* H3K9 monomethylation appears to be prominent in *Z. dumosum* during the wet but not the dry season. Further analysis showed that lack of H3K9 dimethylation is a feature uniquely evolved in the *Zygophyllaceae* family, whose members inhabit dry and semidry regions of the world. We suggest that lessening epigenetic constraints might have an adaptive value providing plants with the capacity of prompt reprogramming of gene expression and quick response to changing environment.