2011 – 2012 Summer Project

Title: Hypertrophic stimuli in cardiomyocytes: effect of natural antioxidants

Laboratory: Epigenomic Medicine

Supervisors: Tom Karagiannis
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Background
Cardiac hypertrophy is an adaptive response to numerous intrinsic and extrinsic stimuli such as excessive aerobic activity or hypertension. It is characterized by increases in cardiomyocyte size and sarcomere organization as well as activation the foetal gene regulatory program. Whereas physiologic hypertrophy is not thought to be harmful, chronic pathological hypertrophy is associated with arrhythmia, heart failure and sudden death. The principle aim of this project is to investigate the effects of the natural antioxidants including coenzyme Q10 and hydroxytyrosol on DNA damage-induced hypertrophy in rat H9c2 rat embryonic ventricular myocytes.

Project Details
In this summer project a well-established cell culture model of cardiac hypertrophy using rat cardiomyocytes (embryonic rat heart derived H9c2 cells) and DNA damage by the cancer chemotherapeutic doxorubicin, which is known to induce double-strand breaks, will be investigated. Furthermore, induction of double-strand breaks by irradiation with 2 Gy γ-rays for which the kinetics of γH2AX formation and disappearance is well-established will be used as a positive control.

The experiments will involve mammalian cell culture and differentiation of myoblasts to skeletal muscle and myocytes, exposure to genotoxic agents and evaluation of the kinetics of γH2AX formation by immunofluorescence by techniques which are well established in the laboratory.

References
2011 – 2012 Summer Project

Title: Dietary histone deacetylase inhibitors in cardiac hypertrophy

Laboratory: Epigenomic Medicine

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Background
Cardiac hypertrophy is an adaptive response to numerous intrinsic and extrinsic stimuli such as excessive aerobic activity or hypertension. It is characterized by increases in cardiomyocyte size and sarcomere organization as well as activation the foetal gene regulatory program. Whereas physiologic hypertrophy is not thought to be harmful, chronic pathological hypertrophy is associated arrhythmia, heart failure and sudden death.

The principle aim of this project is to investigate the effects of the dietary histone deacetylase inhibitors L-sulforaphane and diallyl disulphide on DNA damage-induced hypertrophy in rat H9c2 rat embryonic ventricular myocytes.

Project Details
This summer project forms a part of a larger research direction which is aimed at understanding the genetic and epigenetic mechanisms of cardiomyoblast differentiation and responses to DNA damage. In the project, a well-established cell culture model of cardiac hypertrophy using rat cardiomyocytes (embryonic rat heart derived H9c2 cells) and DNA damage by the cancer chemotherapeutic doxorubicin, which is known to induce double-strand breaks, will be investigated. Furthermore, induction of double-strand breaks by irradiation with 2 Gy γ-rays for which the kinetics of γH2AX formation and disappearance is well established will be used a positive control.

The experiments will involve mammalian cell culture and differentiation of myoblasts to skeletal muscle and myocytes, exposure to genotoxic agents and evaluation of the kinetics of γH2AX formation by immunofluorescence by techniques which are well established in the laboratory.

References

2011 – 2012 Summer Project

Title: Ontogenic and phylogenetic studies: expression of histone deacetylase enzymes

Laboratory: Epigenomic Medicine

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Background
Chromatin undergoes dynamic remodeling to facilitate DNA metabolic processes including transcription, replication and repair. Histone proteins organize the DNA into nucleosomes, the basic repeating units of chromatin. Nucleosomes consist of 146 base pairs of DNA tightly wrapped around a histone octamer consisting of two each of the core histones, H2A, H2B, H3 and H4. It is now well established that post-translational modifications of core histones play a major role in modeling higher-order chromatin structure and controlling gene transcription. Acetylation and deacetylation of the amino-terminal tails of lysine residues are the most well characterized post-translational histone modifications. The opposing actions of two classes of enzymes, histone acetyl-transferases (HATs) and histone deacetylases (HDACs) regulate the acetylation status of the core histones. HDAC enzymes catalyze the removal of acetyl groups from lysine residues resulting in a more compacted, transcriptionally repressed, chromatin structure. Overall, it is proposed that acetylation levels regulate gene transcription by controlling the accessibility of transcription factors to DNA. Controlled equilibrium between histone acetylation and deacetylation is essential for normal cell growth and perturbations in histone acetylation status have been associated with various diseases. Therefore there is an interest in understanding the function and further characterizing the expression of HDAC enzymes.

Project Details
The aim of this project is to evaluate the expression of histone deacetylase enzymes in different vertebrate species and during mammalian development. Immunofluorescence will be the major technique employed in this project.

References