大阪府立大学大学院生命環境科学研究科
獣医学専攻国際オープンセミナー２０１６年度（６）

日時：2017 年 2 月 6 日（月）15 時～17 時
場所：りんくうキャンパス第 1 講義室
演者：カナダ グエルフ大学オンタリオ獣医学部生命医科学講座
Jonathan LaMarre 教授
演題： Small RNAs: Important regulators of gene expression in embryogenesis, biology and disease

大阪府立大学獣医学専攻とカナダグエルフ大学オンタリオ獣医学部(OVC)とは学術交流協定を締結し、これまで 20 年以上に亘り学際的なお付き合いをしています。この度、オンタリオ獣医学部教授 LaMarre 教授を本学に招聘する機会を得ました。博士は、分子病理学を基盤にした遺伝子レベルでの家畜の疾病に関する研究を精力的に進められており、数多くの研究業績を挙げておられます。この度の国際セミナーでは、OVC の教育・研究と馬の臨床の紹介に加え、家畜の生殖器の発生と異常に係る small RNA の機能に関する演題をお願いしました。

OVC は 1862 年に創立され、北米では最も伝統のある獣医学部で、充実した高度な獣医学教育・研究を行っている大学です（http://ovc.uoguelph.ca/）。
動物の疾病の分子病理学に関する研究やグエルフ大学への留学に興味のある学生は奮ってご参加ください。

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Small RNAs: Important regulators of gene expression in embryogenesis, biology and disease

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Extensive research conducted over the past decade has revealed the extraordinary complexity and importance of small RNA pathways in the control of normal development, tissue function and pathologic states, including cellular responses to toxic injury. The majority of this work has focused on changes mediated by the class of small RNAs known as microRNAs (miRNAs), which are single-stranded oligoribonucleotides 19-22 residues in length. MiRNAs mediate their effects by post-transcriptionally targeting specific mRNAs based on complementarity with sequences in the mRNA target. These interactions require microRNA binding to a protein complex known as the RNA-induced silencing complex (RISC), leading to mRNA destruction or translational suppression. More recently, an additional class of small RNAs known as "PIWI-interacting RNAs" (piRNAs) has been implicated in biological processes including reproduction, stem cell biology and cancer. This small RNA pathway utilizes related proteins, known as PIWI proteins, and is best recognized as a genome defense mechanism against retrotransposon expression, although some specific roles in mRNA targeting have recently been proposed. Through binding to retrotransposon or mRNA targets, piRNA/PIWI complexes facilitate RNA decay. In addition, piRNA complexes with PIWIs appear to regulate DNA and histone methylation at specific loci, facilitating epigenetic regulation.

Research in my laboratory has focused on each of these small RNA pathways, primarily in the context of reproduction. Next generation sequencing (NGS) of small RNAs present in animal gametes and gonads has revealed both static and dynamic populations of small RNAs. MicroRNAs including miR-21 and members of the let-7 family are highly abundant in the oocyte, testes and early embryos of one or more species. In the oocyte, miR-21 expression markedly increases during oocyte maturation and early phases of embryo development. Functional studies *in vitro* suggest that this is likely mediated through SMAD and STAT3 binding sites in the promoter of the precursor (primary) miR-21 sequence. Investigation of cellular targets strongly supports previous studies implicating miR-21 in the control of apoptosis pathways. In addition to microRNAs, large numbers of piRNAs were identified in the NGS data. In order to further examine their functions, we mapped the piRNAs to the genome revealing numerous retrotransposon and mRNA sequences. piRNA levels were correlated with turnover of these targets, suggesting important roles in mRNA turnover in gametes and embryos. Finally, we cloned the major PIWI proteins from multiple species in order to characterize their functions in reproduction and cancer. Taken together, our studies implicate small RNA pathways as key regulators of cellular function in gametes and embryos that have the potential to become dysregulated in diseases such as cancer.