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（For JSPS Fellow）

Form B-2
(FY2018)

Date（日付）5/2/2019
（Date/Month/Year:日/月/年）

Activity Report -Science Dialogue Program-
（サイエンス・ダイアログ事業　実施報告書）

- Fellow's name（講師氏名）: Mohammad Mahbubur Rahman（ID No. P17106）

- Participating school（学校名）: Miyazaki Kita Senior High School

- Date（実施日時）:22/1/2019
（Date/Month/Year:日/月/年）

- Lecture title（講演題目）: Study on the molecular bases and prevention of genetic disorders in dogs and cats.

- Name and title of your companying person（講義補助者 職・氏名）
N/A

- Lecture format（講演形式）:
◆Lecture time（講演時間） 80 min（分）, Q&A time（質疑応答時間） 10 min（分）
◆Lecture style（ex.: used projector, conducted experiments）
（講演方法（例:プロジェクター使用による講演、実験・実習の有無など））
Projector and white board

- Lecture summary（講演概要）: Please summary your lecture 200-500 words.

Background: Lysosomal storage diseases (LSDs) are a group of genetic disorders of cellular metabolism which are caused by a deficiency of certain catabolic reaction(s) within the lysosomal catabolic pathway. There are more than 50 disorders in LSDs. Most of the LSDs have a marked pathologic component of central nervous system (CNS), so many of them suffer from severe mental retardation and premature death. GM2 gangliosidosis variant 0 (Sandhoff disease, SD) is a fatal, autosomal recessive, lysosomal storage disorder resulting from excessive accumulation of the GM2 ganglioside in the neurons. The disease is caused by a deficiency of the β-subunit of lysosomal hexosaminidase enzyme due to deleterious mutations of the HEXB gene and

affected individuals die prematurely of brain damage through progressive neurological signs including motor and psycho-intellectual dysfunctions, visual defects, etc.

Objectives: The objectives of my research are clarification of molecular bases of the disease and development of new molecular diagnostic methods aiming to prevent and/or control the disease in dogs and cats.

Methods: Tissue and/or blood samples of suspected animals were collected. DNA and RNA were extracted from the samples with the commercial kits. Conventional PCRs were done to amplify the exonic regions of the HEXB gene and sequencing of the amplified bands were performed. In addition, reverse transcription (RT)-PCR was performed with four overlapping segments of the coding sequences of the gene. Sequencing results of the suspected samples were compared with the reference data in GenBank. After identifying the pathogenic mutations, genotyping methods for canine and feline SD were developed and evaluated.

Results: A novel homozygous single base pair deletion of guanine (c.283delG) was identified in exon 3 in the canine *HEXB* gene in Toy Poodles with SD. In a mixed-breed dog with SD, a novel 20-base pair deletion (c.791_810del20) was identified in exon 8 in the canine HEXB gene. New feline SD was diagnosed with clinical, biochemical and pathological features in a Japanese domestic cat. The feline *HEXB* gene analysis suggested a novel 4-base pair deletion (c.996-23T[7]) at the polypyrimidine tract in intron 9 may cause skipping of exon 10. All assays developed for genotyping the three kinds of mutations were available to discriminate all three genotypes, i.e., wild-type, heterozygous carrier and homozygous mutant genotypes which will be used for diagnosis of suspected cases.

Conclusion: In recessive genetic disorders, carrier animals are clinically healthy but transmit the mutant allele to 50% of their progeny. Therefore, to prevent the spread of the mutation, carrier animals should be neutered and/or excluded from the breeding colony.

- Overall advice or comments to future participants in the program（今後の講師へのアドバイス）:

I appreciate this program. Sometimes students feel difficulties to understand the English.

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- Other noteworthy information（その他特筆すべき事項）:

- Impressions and comments from the accompanying person（講義補助者の方から、本事業に対する意見・感想等がありましたら、お願いいたします。）

If possible , it is better to have accompanying person who are related to same field of research. Although, unfortunately in my case , I missed this oportunity.