✱Medical & Life Science Seminar, 2015 / 平成 27 年度医学・生命科学セミナー✱

Genomic imprinting: Beckwith-Wiedemann syndrome and related disorders

ゲノムインプリンティング ― Beckwith-Wiedemann 症候群と関連疾患 ―

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◆Date: January 13th (WED) from 5:30 p.m. 平成 28 年 1 月 13 日（水）17:30～

◆Place: Lecture room 2, Medical Education & Library Building 3F.

医学教育図書棟 3 階 第 2 講義室

Genomic imprinting is an epigenetic phenomenon that leads to parent-specific differential expression of a subset of genes. Most imprinted genes form clusters or imprinting domains, and are regulated by imprinting control regions (ICRs). Since imprinted genes play an important role in growth and development, aberrant expression of imprinted genes due to genetic or epigenetic abnormalities is involved in the pathogenesis of many human disorders. For example, androgenetic cells lack the expression of all maternal expressed genes and this leads to complete hydatidiform mole, whereas parthenogenetic cells lack the expression of all paternal expressed genes, which leads to ovarian teratomas. Beckwith-Wiedemann syndrome (BWS) is a representative imprinting disorder characterized by macrosomia, macroglossia, abdominal wall defects, and a predisposition to tumorigenesis. The relevant imprinted chromosomal region in BWS is 11p15.5, which consists of two imprinting domains: *IGF2*/*H19* and *CDKN1C*/*KCNQ1OT1*. BWS has five known causative epigenetic and genetic alterations: loss of methylation (LOM) at *Kv*DMR1, gain of methylation (GOM) at *H19*DMR, paternal uniparental disomy, *CDKN1C* mutations, and chromosomal rearrangements. Opposite methylation defects, GOM and LOM, at *H19*DMR are known to cause clinically opposite disorders: BWS or Silver-Russell syndrome (SRS), respectively. In addition, a recent study discovered that loss of function or gain of function of *CDKN1C* also causes clinically opposite disorders: BWS or IMAGe syndrome (Intrauterine growth restriction, metaphyseal dysplasia, adrenal hypoplasia congenita, and genital anomalies), respectively. To date, we have analyzed approximately 200 BWS patients and revealed the frequency of each causative alteration. We have found several related pathological conditions among BWS patients. These are multiple methylation defects (MMDs), which show aberrant methylation at imprinted loci other than 11p15.5, mosaicism of paternal uniparental diploidy (PUD mosaicism), i.e., androgenetic/biparental mosaicism, and placental mesenchymal dysplasia (PMD). In this seminar, I will present the latest research into the imprinting mechanism of 11p15.5, the epigenetic and genetic etiologies of BWS, and the related pathological conditions including SRS, IMAGe syndrome, MMDs, PUD mosaicism, and PMD.

●Inviter: Prof. H. Katabuchi (Dept. of Obstetrics & Gynecology) 産科婦人科学分野 片渕 秀隆 教授

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