東北大学グローバルCOE

Network Medicine 創生拠点

大学院セミナー

鈴木　拓児 博士

(Division of Pulmonary Biology,
Cincinnati Children's Hospital Medical Center・客員研究員)

Recessive GM-CSF receptor alpha(*CSF2RA*) mutations cause hereditary pulmonary alveolar proteinosis

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Primary pulmonary alveolar proteinosis (PAP) is a rare syndrome characterized by accumulation of pulmonary surfactant resulting in respiratory insufficiency. Current concepts of pathogenesis draw from the discovery of PAP in mice deficient in granulocyte/macrophage-colony stimulating factor (GM-CSF), and the strong association of GM-CSF autoantibodies with the common clinical form, representing 90% of cases. We recently identified a new genetic disease associated with mutations of in *CSF2RA,* the gene encoding GM-CSF-Rα and located in the pseudoautosomal region on X and Y chromosomes. These patients present with progressive dyspnea of insidious onset in previously healthy children who develop GM-CSF autoantibody negative PAP. Using elevated serum GM-CSF as a disease-specific biomarker present in the first case, we identified 7 more cases located throughout the world. Diverse *CSF2RA* mutations were identified, including point mutations (G196R), nonsense mutations (R217X), duplications (920dupGC), exon deletion and splicing mutations (ΔExon 7), and gene deletions (XpΔ1.6). All impaired the binding and clearance of GM-CSF, GM-CSF receptor signaling, and GM-CSF-dependent leukocyte functions. Serum surfactant protein D and GM-CSF were elevated, providing useful measures of lung disease severity. These results demonstrate that were elevated, critical for surfactant homeostasis in humans and that mutations in *CSF2RA* cause congenital PAP.

本セミナーは医学履修課程特別セミナー等を兼ねています。受講学生は履修簿を持参し、セミナー修了後にサインを受けること。聴講は自由大歓迎です。学部生の皆さんもぜひどうぞ。

拠点リーダー **岡　芳知** ／ 世話人 **貫和　敏博**（呼吸器病態学分野・内線8539）