

during the proliferative phase, but decreased in the secretory phase. Observation of the phosphorylated ER α revealed that while the expression of p-ER α (Ser 104) was constant, p-ER α (Ser 118) was shown following a cyclic pattern like that of the p-AKT1/2/3 (Thr 473).

To reveal the difference between normal and cancerous glandular cells, cultured Ishikawa cells were first examined immunohistochemically. The expression pattern of phosphorylated ER α and AKT in the untreated Ishikawa cells was similar to that of the normal endometrial cells, except that the expression of p-ER α (Ser 167) was only found in Ishikawa cells. Following treatment with various inhibitors that specifically target the ErbB/PI3K/AKT pathway, it was found out that the expression of p-ER α (Ser 118) and p-ER α (Ser 168) was inhibited. Further examination showed that inhibition of PI3K or AKT, rather than ErbB could induce apoptosis, which could be antagonized by the addition of estrogen, indicating a mitochondrial pathway is involved. Further study is necessary to explore functional difference of ErbB/PI3K/AKT in normal and cancerous endometrial cells.

P2-05

デュシェンヌ型筋ジストロフィーモデルマウスの腎機能評価

(病態生理学)

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デュシェンヌ型筋ジストロフィー (DMD) は最も頻度が高く、かつ重篤な遺伝性筋疾患である。根本的な治療法は確立されていないが、心筋保護治療法によって患者の寿命は飛躍的に延びている。一方、大多数の患者が骨密度低下による骨粗鬆症や骨折を経験する。さらに患者の高齢化に伴い腎機能低下などの多臓器不全が新たな合併症として報告されている。低分子プロテアーゼインヒビターである cystatin C の血清値が筋肉量に影響を受けないことから、筋疾患患者における腎機能の評価に有用であることが報告された。DMD モデルマウスである mdx は筋症状をよく反映しており骨代謝についても研究が進んでいるが、腎機能について詳細な検討がなされていない。本研究では、mdx マウスの腎機能

を評価するとともに、筋ジストロフィー症状との関連を明らかにすることを目的とした。さらに、摂取する食餌のリン含有量を変化することで mdx マウスのリン代謝と骨代謝への影響を検討した。その結果、mdx マウスの血中 cystatin C 値は6週齢頃までは野生型マウスと差はないものの、9週齢頃から上昇し、12週齢では有意差をもって高値となった。 μ CT スキャンを用いた腎機能解析の結果、12週齢の mdx マウスは造影剤のクリアランスが遅延することが明らかとなった。一方、筋損傷の指標となる血中クレアチンキナーゼ値と cystatin C 値に相関は認められなかった。しかし、9週齢から12週齢にかけては筋損傷が増悪化する第2次筋損傷期であることから、腎機能は筋損傷の繰り返しが起因していると示唆された。また、高リン食を摂取した mdx マウスで、血中リン酸値や PTH 値が野生型と比較して有意に増加したものの、骨形成マーカーである血中 BALP 値は有意に減少するという bone uncoupling が生じた。mdx マウスは筋症状に加えて骨密度の低下が認められるが、今回の結果において腎機能低下が骨密度低下の一要因になることが示唆された。

P2-06

Immunohistochemical study of cell differentiation and microvessel property in human mucosa with tooth marks

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Angiogenesis is an important issue related to normal growth and differentiation. In irregularly forms of oral mucosa, angiogenesis is a critical issue in the progression of human disease. The tooth marks occur after pressing the teeth for a long period under muscle tension in the human oral cavity. However, this site of

angiogenesis, cell differentiation and microvessel density is not known in the human mucosa. Therefore, we investigated the relationship of differentiation (Ki-67,) and angiogenesis markers (CD31, D2-40, VEGF-A) in the second molar region of oral mucosa in dentulous group with tooth marks using immunohistochemical methods compared to that of edentulous. In this result, developed vessels and lymphatic vessels were found in irregular mucosa and the development of these vessels in the oral mucosa provided specific histological information on future tumor progression.

P2-07

Utility of Implantable Cardiac Monitoring System for detecting cardiac arrhythmias in patients with unexplained syncope

(循環器内科学)

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【Introduction】 Although risk of death in patients with cardiac syncope is double compared to the general population, identifying the cause of syncope is very challenging. The implantable Cardiac Monitoring (ICM), which can continuously monitor and store ECG recordings, was invented. Utility of ICM for patients with syncope has not been thoroughly investigated.

【Methods】 We conducted a prospective Multi-Centre observational study in 120 patients (mean age 68±16 years, 80 males) implanted with ICM for unexplained syncope between 2011 and 2018. We assessed the diagnostic yield and elapsed time for diagnosis of syncope.

【Results】 During the mean follow-up period of 18±19 months, causes of syncope were diagnosed in 37% of all patients. The causes of syncope were sick sinus syndrome (77%), paroxysmal atrioventricular block (7%), tachycardia (9%), and others (7%). The mean period from the first episode of syncope to ICM implantation was 30±71 months (range 0-490). And the period from implantation to diagnosis was 4±5 months (range 0-20).

【Conclusions】 ICM was useful to diagnose unex-

plained repetitive syncope. It was a relatively long process for patients with syncope from the first episode of symptoms to ICM implantation. Early implantation of ICM should be considered in patients with undefined cause of syncope by standard diagnostic process. Further study is needed to investigate whether the strategy of initial ICM implantation would provide a more accurate diagnosis than a conventional strategy.

P2-08

Different ECG Changes of CRBBB with Time between Health Check-up Examinees and Patients with Cardiac Diseases

(循環器内科)

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【Purpose】 CRBBB is benign arrhythmia, but an its association with risk for cardiovascular or total death was reported. We investigated the changes of CRBBB ECG during follow-up in healthy and diseases subjects.

【Subjects and Methods】 As a control, 80 CRBBB individuals at the health check-up (55.1±10.8 yrs, male 81.3%) and 50 patients with cardiac diseases (60±8 yrs, male 92%) were included, and the ECG changes were compared during follow up >3 years.

【Results】 At baseline, there were significant differences in PR interval, QRS width and QTc between control and patient group : 165 ±21 vs. 181±29 ms, 141±13.0 vs. 156±18 ms and 419±19 ms vs. 444±33 ms ($P<0.001$ for all), respectively. During the follow-up, QT and QTc prolonged in the control : 415±29 ms to 423±28 ms and 419±19 ms to 424±21 ms ($P<0.01$). Prolonged QRS width >10 ms during follow up was more frequent found in the patient group than the control (9.8% vs. 1.3%, $P=0.016$). Normalization of QRS was observed in 6.1% and 7.8% for control and patients ($P=0.713$).

【Conclusion】 QRS and QTc were prolonged, and widening of QRS occurred more often in the patient group. The significance of the different ECG changes during follow-up need to be determined.