

大学院博士前期課程臨床検査学専攻「先端医学論」の授業紹介

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先端医学論はオムニバス形式で、各教授がそれぞれ注目されている先進医学のトピックスなどを紹介し、課題や将来への展望を学習・議論する事で、医療現場への応用・対応ができる資質を高める科目です。今回は私が担当した授業を紹介します。

私が紹介した論文は、High Density Lipoprotein(HDL)に関する論文で、HDL 機能として重要なコレステロール引き抜き能力を簡便に測定する方法の論文です。このような論文を材料に、新規性・有用性・問題点について討論する事で、臨床検査として医療現場への適応させる事への応用や対応が可能となります。

ARTICLES

Cholesterol Uptake Capacity: A New Measure of HDL Functionality for Coronary Risk Assessment

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Background: Recent studies have shown that the cholesterol efflux capacity of HDL is a better predictor of cardiovascular disease (CVD) than HDL cholesterol. However, the standard procedures used for measuring cholesterol efflux capacity involve radioisotope-labeled cholesterol and cultured macrophages. Thus, a simpler method to measure HDL functionality is needed for clinical application.

Methods: We established a cell-free assay system to evaluate the capacity of HDL to accept additional cholesterol, which we named cholesterol "uptake capacity," using fluorescently labeled cholesterol and an anti-apolipoprotein A1 antibody. We quantified cholesterol uptake capacity of apolipoprotein B (apoB)-depleted serum samples from patients with coronary artery disease who had previously undergone revascularization.

Results: This assay system exhibited high reproducibility (CV < 10%) and a short processing time (< 6 h). The myeloperoxidase-mediated oxidation of apoB-depleted serum impaired cholesterol uptake capacity. Cholesterol uptake capacity correlated significantly with cholesterol efflux capacity ($r^2 = 0.47$, $n = 30$). Furthermore, cholesterol uptake capacity correlated inversely with the requirement for revascularization because of recurrence of coronary lesions in patients with optimal control of LDL cholesterol ($P < 0.01$, $n = 156$). A multivariate analysis adjusted for traditional coronary risk factors showed that only cholesterol uptake capacity remained significant (odds ratio, 0.48; 95% CI, 0.29–0.80; $P = 0.0048$).

Conclusions: Cholesterol uptake capacity assay evaluates the functionality of HDL in a sensitive and high-throughput manner without using radioisotope label and cells. This assay system could be used for the assessment of CVD risk in the clinical settings.

IMPACT STATEMENT

This article will benefit patients with optimal control of LDL cholesterol that need an alternative marker for recurrence risk of coronary artery disease. This cell-free assay system for measuring cholesterol uptake capacity will allow high-throughput characterization of HDL functionality with a tiny amount of apoB-depleted serum. The information presented here will contribute to advancement of dysfunctional HDL research and development of drugs with novel mode of action to reduce the residual risk of cardiovascular disease by improving HDL functionality.

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