BIOCHEMICAL LETTERS

β -Migrating very-low-density lipoprotein, chylomicron remnants and their receptors

Voorschuur et al. [1] recently published in the Biochemical Journal a paper about the different zonal distributions of the asialoglycoprotein receptor, the low-density lipoprotein (LDL) receptor-related protein (LRP) and the lipoprotein remnant receptor of rat hepatocytes. β -Migrating very-low-density lipoprotein (β -VLDL) was used as the ligand for determination of the lipoprotein remnant (apoE) receptor to their experiments. Because of the affinity of β -VLDL for several lipoprotein receptors, the β -VLDL binding assay cannot be (simply) referred to as binding of β -VLDL to the lipoprotein remnant receptor.

The concept of an independent lipoprotein remnant receptor comes from the observations on LDL-receptor-deficient subjects. However, there is no general agreement on the nature of this receptor. Several receptors have been considered to be involved in clearance of lipoprotein remnants, including LDL (apoB, apoE) receptor, LRP, VLDL receptor and asialoglycoprotein receptor. Among them, the importance of the LDL receptor for removal of lipoprotein remnants is well established. The ligands for the LDL receptor among natural lipoproteins are apoB100 and apoE. The LDL receptor recognizes not only apoB100-containing lipoproteins (LDL), but also apoE-containing lipoproteins such as apoE-containing high-density lipoprotein, VLDL, β -VLDL and chylomicron remnants.

Both chylomicron remnants and β -VLDL are the ligands for the LDL receptor. Although several studies have demonstrated the existence of LDL-receptor-independent, Ca^{2+} -independent, binding sites for lipoprotein remnants in hepatocytes [2–5], chylomicron remnants and β -VLDL are shown to bind to the same recognition site, i.e. the LDL receptor, on liver membranes and hepatocytes, macrophages and other cells, as demonstrated *in vitro* by ligand competition, receptor blockage by anti-(LDL receptor) antibodies, ligand blots and immunoblots [2–9]. The LDL receptor is also the principal binding site of the liver responsible for remnant removal *in vivo* [6,7,10].

LRP has been proposed as a candidate for the remnant receptor. LRP is involved in clearance of chylomicron remnants in LDL-receptor-deficient mice, but plays a lesser role in normal mice [10]. The recently cloned VLDL receptor is a specific apoE receptor, as this receptor recognizes VLDL and β -VLDL, but not LDL [11]. However, this receptor is expressed in heart, muscle and adipose tissues, but is scarcely expressed in the liver. The significance of the VLDL receptor *in vivo* is currently unclear. The asialoglycoprotein receptor, which is exclusively expressed in liver, has also been proposed to play a possible role in clearance of lipoprotein remnants, as asialoglycoproteins compete binding to hepatocytes *in vitro* with chylomicron remnants [12].

The basis for Voorschuur et al. [1] to use β -VLDL for determination of the lipoprotein remnant receptor of rat hepatocytes is that β -VLDL and chylomicron remnants bind to this elusive remnant receptor. As described above, β -VLDL and chylomicron remnants largely bind to LDL receptor, which

is especially well documented in rat liver membranes and hepatocytes.

Therefore, the β -VLDL binding assay in hepatocytes represents largely binding of β -VLDL to the LDL receptor, rather than to the distinct remnant receptor.

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β -Migrating very-low-density lipoproteins and chylomicron remnants bind to rat liver hepatocytes at a low-density-lipoprotein-receptor-independent site (the remnant receptor)

Dr. Wei Liao [1] is quite right in establishing that the receptors involved in recognition of β -migrating very-low-density lipoproteins (β -VLDL) and chylomicron remnants are subject to a lively international debate. During the last American Heart Association Meeting (November 1994, in Dallas, TX, U.S.A.) the Council on Arteriosclerosis supported a Featured Research session on 'Lipoprotein Remnant Removal' summarizing the