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Action of Lipoprotein Lipase on Apoprotein-Depleted Chylomicrons

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1. Rat lymph chylomicrons were exposed to soluble and to immobilized trypsin. This treatment caused no detectable changes in the chylomicron structure or lipid composition, but did result in virtually total depletion of all their tetramethylurea-soluble apoproteins. 2. The capacity of these apoprotein-depleted chylomicrons to act as substrate for lipoprotein lipase *in vitro* and *in situ* (i.e. isolated perfused rat heart) was decreased by about 90 and 75% respectively, compared with intact chylomicrons. 3. On incubation with rat plasma high-density lipoproteins, trypsin-treated chylomicrons readily acquired a full apoprotein complement. This resulted in the complete restoration of their capacity to act as substrate for lipoprotein lipase both *in vitro* and *in situ*. 4. It is suggested that with the use of trypsin-treated chylomicrons it is now possible for the first time to investigate the physiological role that individual apoproteins play in the catabolism of triacylglycerol-rich lipoproteins by lipoprotein lipase.

The initial event in the catabolism of plasma chylomicrons and VLD lipoproteins is the hydrolysis of their triacylglycerol moiety by lipoprotein lipase (Robinson, 1970). Suggestions have been made that the rate of this hydrolysis may be modulated by some of the polypeptides normally present on the surface of these lipoproteins (Krauss *et al.*, 1973; Bar-On *et al.*, 1976; Schonfeld *et al.*, 1976; Rogers *et al.*, 1976). These suggestions are based on observations carried out *in vitro*, which showed that various apoproteins (apoproteins C, A and E) can affect the hydrolysis of artificial triacylglycerol emulsions by solubilized lipoprotein lipase (La Rosa *et al.*, 1970; Havel *et al.*, 1970; Brown & Baginsky, 1972; Havel *et al.*, 1973*a*; Krauss *et al.*, 1973; Miller & Smith, 1973; Bensadoun *et al.*, 1974; Östlund-Lindqvist & Iverius, 1975; Ganesan & Bass, 1975; Ekman & Nilsson-Ehle, 1975; Ganesan *et al.*, 1976; Quarfordt *et al.*, 1977). There seems to be a general agreement from these studies that apoprotein C-II has an activating effect on the hydrolysis. The role of the other apoproteins is less clear. For example, apoprotein C-I and apoprotein C-III have been variously described to have activating or inhibitory effects on the hydrolytic reaction (La Rosa *et al.*, 1970; Havel *et al.*, 1970; Ganesan *et al.*, 1971; Brown & Baginsky, 1972; Havel *et al.*, 1973*a*; Bensadoun *et al.*, 1974; Ganesan & Bass, 1975; Östlund-Lindqvist & Iverius, 1975).

Abbreviations used: VLD lipoprotein, very-low-density lipoprotein; LD lipoprotein, low-density lipoprotein; HDL lipoprotein, high-density lipoprotein.

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The reasons for these differences have been ascribed to variations in the purity of the polypeptides and to the nature of enzyme preparations used (Havel *et al.*, 1973*a*). These have included purified as well as crude lipoprotein lipase preparations from post-heparin plasma (Havel *et al.*, 1973*a*; Ganesan & Bass, 1975; Ganesan *et al.*, 1976), adipose tissue (Havel *et al.*, 1973*a*; Krauss *et al.*, 1973; Ekman & Nilsson-Ehle, 1975), human and cow's milk (Havel *et al.*, 1970, 1973*a*; Miller & Smith, 1973; Östlund-Lindqvist & Iverius, 1975) and rat heart (Twu *et al.*, 1975; Chung & Scanu, 1977). In addition, differences in the substrate preparation could also account for the variations in results. Studies have shown that the hydrolytic activity of soluble lipoprotein lipase on emulsified triacylglycerol can be affected by the concentration and type of emulsifying agent used (e.g. phospholipids, Triton, gum arabic) (Chung *et al.*, 1973; Blaton *et al.*, 1974; Riley & Robinson, 1974; Heaf & Carlson, 1976). In view of these limitations, it is apparent that no assertions can yet be made about the role that the C apoproteins, as well as other apoproteins, singly or combined, may have in the hydrolysis of chylomicrons or VLD lipoprotein triacylglycerol, the physiological substrates for lipoprotein lipase.

The present investigation was initiated to examine the possibility of using chylomicrons to study the effects of C apoproteins on the catalytic action of lipoprotein lipase. The use of this substrate is complicated, however, by the fact that it already possesses these apoproteins. To avoid this problem, chylomicrons were treated with trypsin, which, under appropriate conditions, depleted the apoproteins