Hypercholesterolemia: So much cholesterol, so many causes

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Hypercholesterolemia is a disease characterized by excess cholesterol in the blood. Often there are no apparent symptoms, with a blood test being the only way to detect high cholesterol. Hypercholesterolemia has several causes, the most common being a diet including many foods containing saturated fats and cholesterol. Obesity and underlying diseases such as diabetes mellitus and liver dysfunction, as well as mutant genes affecting cholesterol metabolism also cause hypercholesterolemia. The latter forms are known as Familial Hypercholesterolemia (FH), and have been well studied and are the focus of this review. With FH, the physical symptoms are severe, involving visible accumulations of cholesterol throughout the body. Autosomal dominant mutations affect low-density lipoprotein receptors (LDLR). Mutant apolipoprotein, mutant adaptor protein, and mutant ABC transporters, which causes a sister disease *Sitosterolemia*, also lead to FH. Experiments over the past fifteen years have illuminated both the molecular basis of this disease as well as the biology underlying endocytosis. Currently a change in diet, surgery to remove cholesterol deposits, and several cholesterol-lowering drugs are the methods used to treat FH. Possible treatments in the future include gene therapy using adenoviruses.

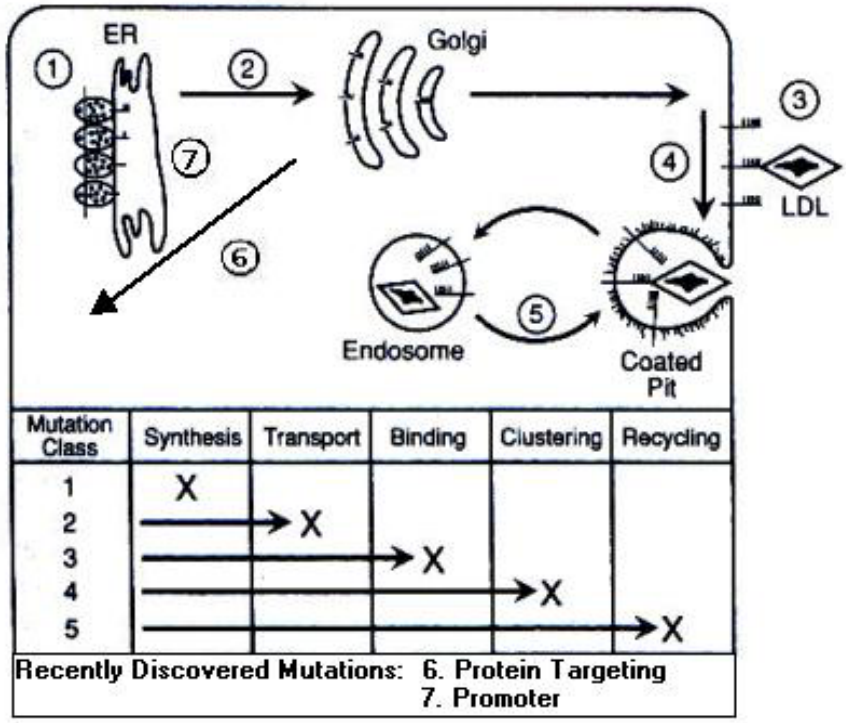

Figure 1: Autosomal Dominant Mutations of LDLR.

This figure illustrates the various ways that a defect in receptor can occur. In addition to these mutations, an autosomal dominant mutation of apolipoprotein and autosomal recessive mutations in cholesterol excretion and adaptor proteins also genetically cause Hypercholesterolemia. (*Figure adapted from Goldstein et al.*[1] Familial Hypercholesterolemia)