The effects of TZDs are probably due to the remodeling of adipose tissue and increased adiponectin secretion.

**SUMMARY**

**Studying the pathogenesis of insulin resistance and the role of PKC in insulin resistance**

- In HHTg rats, elevated serum triglycerides and FFA were associated with the ectopic accumulation of triglycerides in tissues and reduced insulin sensitivity of peripheral tissues. Impaired glucose utilization in the peripheral tissues was associated with the reduced activity of GS in skeletal muscle. Decreased GS activity and glucose utilization in peripheral tissues indicate a possible defect in insulin signal transduction. In line with this, our results show that skeletal muscle IR was associated with the increased activation and translocation of PKC θ.

- Nutritionally induced obesity of HHTg rats resulted, in many cases, in the further deterioration of metabolic abnormalities associated with IR. We found that PKC θ, in particular, could contribute to the metabolic abnormalities associated with IR and obesity.

- The age-related increase in IR and deterioration of some parameters of carbohydrate and lipid metabolism, were not associated, in HHTg rats, with obesity but with increased serum levels of triglycerides and FFA.

- The age-related worsening of IR in HHTg rats was accompanied by increased relative amounts of PKC θ in skeletal muscle. These findings...
suggesting the possible involvement of PKC θ in skeletal muscle IR disorders.

**Studying the potential role of resistin in the pathogenesis of insulin resistance**

- The chronic transgenic expression of resistin in adipose tissue in SHR rats was associated with disorders of lipid and carbohydrate metabolism, the resistance of adipose tissue to insulin action and a significant increase in the relative amount of PKC θ in skeletal muscle.

- The results support the hypothesis of a role of resistin in the mechanisms underlying IR, suggesting its autocrine effects on adipose tissue. Whether PKC may play a role in the deterioration of metabolic abnormalities, which is accompanied by the increased expression of resistin in adipose tissue, was not completely resolved.

**Effects of pharmacological intervention in insulin resistance**

- Long-term pioglitazone treatment positively influenced the metabolic abnormalities associated with IR. It decreased the serum concentrations of triglycerides and FFA, increased the insulin sensitivity of adipose and muscle tissue, increased the serum levels of adiponectin and avoided the development of hyperinsulinemia. By contrast, pioglitazone increased skeletal muscle triglyceride accumulation and activated PKC ε and PKC θ.

- The beneficial effects of TZDs can be explained by the remodeling of adipose tissue and increased adiponectin secretion.