

Comparative evaluation of gene delivery devices in primary cultures of rat hepatic stellate cells and rat myofibroblasts

ABSTRACT

The results suggest FuGENETM6-based techniques can be optimized to provide a practical means of gene transfer into rat (not shown in this article) hepatic stellate cells, and that the use of "adenoviral-mediated" transfer is also proving effective for gene delivery to these cellular targets.

INTRODUCTION

The association between atherosclerosis and coronary heart disease (CHD) in developed nations has been a major factor in morbidity and mortality. However, the low mortality rate of CHD in France, particularly the southwest region, is an exception. This phenomenon, known as the French paradox, may be linked to excessive red wine consumption. It has been 25 years since the first study linked alcohol consumption to CHD, and a significant inverse relationship between the two has emerged through numerous studies. In vivo studies have revealed that red wine consumption is more effective in preventing CHD than other forms of alcoholic beverages. Hence, it has been hypothesized that naturally occurring elements in wine could provide protection against CHD by targeting specific sites involved in the etiology of CHD, such as soluble blood components (LDL), cellular blood elements (platelets), or the vasculature (endothelium). According to Siemann and Creasy, trans-resveratrol, a tri-hydroxy stilbene found in red wine, is known to have cardioprotective effects, inhibit LDL oxidation, suppress smooth muscle proliferation, induce nitric oxide synthase expression, and hinder collagen-induced aggregation responses in washed platelets. Nevertheless, the impact of resveratrol on vascular components, particularly the endothelial cells, which are crucial for the maintenance and function of the arteries, intestines, and lungs, has been little researched. The impact of nutritional status and certain foods on the homeostasis of the vascular endothelium, as well as other metabolic and physiologic activities, can be determined. Our study revealed that resveratrol caused significant cellular and biochemical changes in endothelial cells, which were accompanied by altered functional responsiveness to simulating arterial flow. We tested the same set of biochemical parameters in resveratrol-treated cells, as previous studies have revealed several changes in signaling molecules due to endothelial cell cytoskeleton reassemblance to arterial shear stress. The use of selective signaling pathway inhibitors enabled the demonstration that cytoskeletal changes induced by resveratrol were dependent on intracellular calcium and tyrosine kinase activity changes, and also appeared to be linked to the integrity of actin microfilaments and microtubule network. A mechanism that is similar to the one triggered by shear stress may act as the mechanism by which resveratrol functions.

CONCLUSION

Results: Traces of the mRNA differential display were used to identify genes with altered expression in *Pneumocystis carinii*-infected hosts, and the exact sequence of one of these fragments (gene encoding the mitochondrial ATPase 6 of F₀F₁, a subunit of this complex) was found to be homologous to the nucleotide of an expressed gene). The ATPase 6 gene is overexpressed during *P. carinii* infection, as indicated by the northern blot analysis of total RNA extracted from rat lung infected with PCA and mock-infused rabenoviruses. By in situ hybridization of cells

found to be distal and apical of the respiratory tree and of alveoli that expressed the phosphatases 6 and 8 gene, it was shown that these regions were more than 120 genes and some of those on the distal parts of mice mice. The over-expression of the ATPase 6 gene in *P. carinii* infection is thought to be caused by type II pneumocytes and Clara cells, as indicated by the presence of SP-B gene expressed through a two-color fluorescent in situ hybridization.