## PREFACE

The research presented in this thesis started with studying the effects of oxidative stress in transplanted solid organs including kidneys. Immunosuppressive therapy with cyclosporin A (CsA) in order to prevent the rejection of transplanted organs is accompanied by undesired effects that promote a decline of the transplant function and accelerated atherogenesis. We hypothesized that CsA inhibits the mitochondrial permeability transition pore (MPTP). Inhibition of the MPTP will result in an increased mitochondrial membrane potential. Mitochondrial respiration was expected to proceed with an increased production of oxygen free radicals. In chapter 6 of this thesis we described that blocking of the MPTP did not play a role in CsA-induced oxidative stress. An important and unexpected result of this project stems from our use of cigarette smoke (CS) as a positive control for oxidative stress as shown in figure 1.

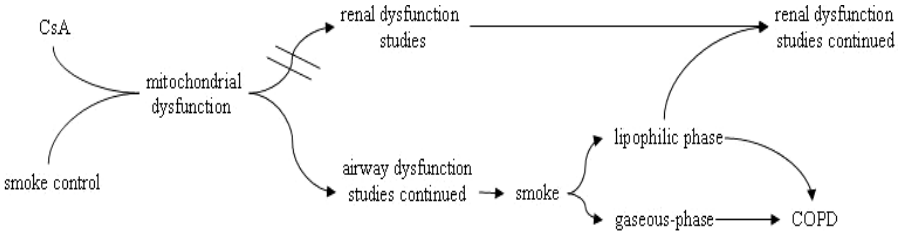


**Figure 1.** Incidence and significance of serendipity findings.

These serendipitous findings, described in chapter 1, showed that CS disturbs mitochondrial function, thereby decreasing the capacity of mitochondria for adenosine triphosphate synthesis, leading to increased susceptibility for cellular necrosis. We thought that it would be of interest to continue studying the effects of CS on airway epithelial cells. Finally, the results described in this thesis are of importance for both chronic obstructive pulmonary disease (COPD) and renal dysfunction after transplantation as described in the summary and future perspectives.