J. Biol. Res. 2011 n.1 - Vol. LXXXIV - Rubbettino - Soveria Mannelli

# Protective effects of Resveratrol in an experimental model of abdominal aortic aneurysm induction

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KEY WORDS: Abdominal aortic aneurysm, Monocytes, MMPs, TNF-α

## Abstract

***Resveratrol (Rsv) is a natural antioxidant polyphenol with vasoprotective properties. We evaluated whether Rsv affects the inflammatory response in an experimental model of elastase-induced abdominal aortic aneurysm. Thirty male rats were subjected to aneurysm induction and treated or not with Rsv. Circulating levels of CD62L- monocyte subset, monocyte CD143 surface expression, MMP-9 plasma activity and TNFα serum levels were lower in Rsv-treated rats. In conclusion, Rsv acts as an anti-inflammatory compound and could be of great relevance to improve the immune response in AAA patients.***

## Introduction

Abdominal aortic aneurysm (AAA) is a degenerative disease characterized by inflammatory infiltrate and degradation of structural extracellular matrix protein [1]. The rat CD62L- monocytes are involved in the early inflammatory response, differentiate into tissue macrophages and produce TNFα. Studies indicated a pathogenetic role for TNFα in AAA. Moreover, monocytes secrete the proteolytic enzyme MMP-9 which results overexpressed in tissue and plasma of AAA patients. Finally, CD143/ACE promotes the renin-angiotensin system-dependent pro-oxidant bursts and, thus, its alterations might represent a sign of AAA progression. Rsv is a dietary polyphenol with cardiovascular protective effects [2]. We used the *in situ* elastase infusion model in rat to induce aneurysm [3] and to verify the effects of Rsv on aneurysm-associated inflammation.

## Materials and Methods

### *Experimental Model of Abdominal Aneurysm*

15 male Sprague Dawley rats were treated with Rsv per os (10 mg/kg/die) (Rsv, n=15) or vehicle alone (Ct, n=15). After 7 days of treatment, all rats were subjected to AAA induction as described [3]. After 14 days, serum or plasma were collected.

### *Flow cytometry*

Lysed blood cells were incubated with CD143-FITC (GeneTex), CD11b/c-PE (BioLegend), CD62L-PerCP (BioLegend) and run on a FACSCalibur flow cytometer and analyzed by CellQuest software.

### *Zymography for plasma MMP-9 activity*

Equal amounts of plasma were run on a gelatin casted gel. Plasma MMP-9 activity was evaluated by optical densitometry of gelatinolytic bands (gel analysis system GeneGenius, Syngene).

### *TNFα serum levels*

TNFα serum levels were measured by Elisa immunoassay according with manufacturer instructions (Bender Med System).

### *Statistical analysis*

The data were analyzed using unpaired Student's t-test. Normally distributed values are described as means ± SEM.

## Results

Compared to control animals, Rsv treatment decreased the rate of the CD62L- monocyte fraction (Figure 1A) and the surface level of CD143 (Figure 1B).

AAA rats treated with Rsv had a lower level of circulating MMP-9 (Figure 2A) and TNFα (Figure 2B) than untreated rats.

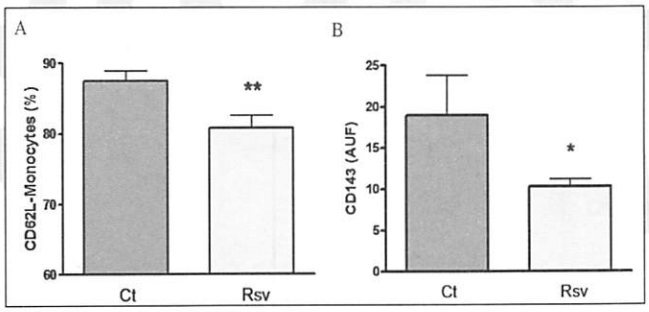


*Figure 1. Flow cytometric analysis of CD62L- monocyte percentage (A) and monocyte surface level of CD143 (B) in rats with elastase-induced AAA. ** p<0.01vs Ct; * p<0.05vs Ct.*

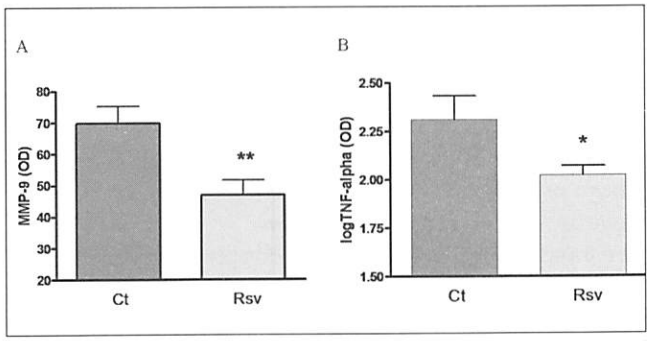


*Figure 2. (A) densitometric analysis of plasma MMP-9 activity determined on gel zymography; (B) TNFα serum content determined by ELISA assay: ** p<0.01vs Ct; * p<0.05vs Ct.*

## Discussion

Rsv is a dietary polyphenolic antioxidant compound. Using an experimental model of AAA induction, we demonstrated that Rsv is able to decrease the percentage of the monocyte subset involved in the early inflammatory response. Rsv also decreases TNFα serum level, MMP-9 plasmatic activity and CD143 monocyte expression. The differentiation of monocytes into macrophages is accompanied by a dramatic increase in CD143 expression and in cytokines and protelolytic enzymes production. Thus, our *in vivo* results suggest that anti-inflammatory properties of Rsv, operative in aortic injury, depend on the modulation of monocyte differentiation and of their madiators interferering finally with the proteolytic mechanism responsible for AAA progression. Further studies are requested to evaluate whether Rsv use may play a role in the care of patients with AAA.

## References

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