# Polymorphisms of receptor for advanced glycation end-products (RAGE) and glyoxalase I genes in patients with clear cell renal cell cancer

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## *Introduction:*

The receptor for advanced glycation end-products (RAGE), a member of the immunoglobulin super-family, takes part in the pathogenesis of many diseases, including cancer. RAGE is multi-ligand receptor (Fig. 1), binding advanced glycation end products (AGE) and mediators like proinflammatory S100 proteins/calgranulins, High Mobility Group proteins including HMGB1/amphoterin and amyloid β peptid. RAGE-ligand interaction is followed by generation of oxidative stress and triggering of inflammatory and proliferative processes which critically contributes to tissue injury. AGEs have many pathological effects and may contribute to malignancies. Stimulation of RAGE probably potentiates the process of growth, infiltration and metastasis of tumor. AGE-precursors are detoxified by glyoxalase I (GLO I) and decreased glyoxalase I activity due to the aging process and oxidative stress result in increased glycation and tissue damage.

The aim of the study was to find out the relationship between polymorphisms of RAGE (AGER) and GLO I genes and the risk of ccRCC.

## *Methods:*

The studied group consisted of 214 patients with ccRCC and 154 controls. All polymorphisms (RAGE -429T/C, -374T/A, 2184A/G, G82S and GLO I A419C) were determined by PCR-RFLP and confirmed by sequencing. Chi2-squared test or Fisher exact test were used comparison of proportion and for testing of Hardy Weinberg equilibrium.

## *Results:*

We found out the difference in allelic and genotype frequencies in GLO I /A419C/ polymorphism among studied groups (p = 0.02). The relationship between Fuhrman grade 4 of the ccRCC and RAGE gene polymorphism -429T/C, -2184A/G was detected (p < 0.008). We did not show any difference in allelic and genotype frequencies in other RAGE polymorphisms among the studied groups. Genotype frequencies of each polymorphism, except RAGE -429 T/C in patient with ccRCC, correspond to expected frequencies according to Hardy-Weinberg equilibrium.

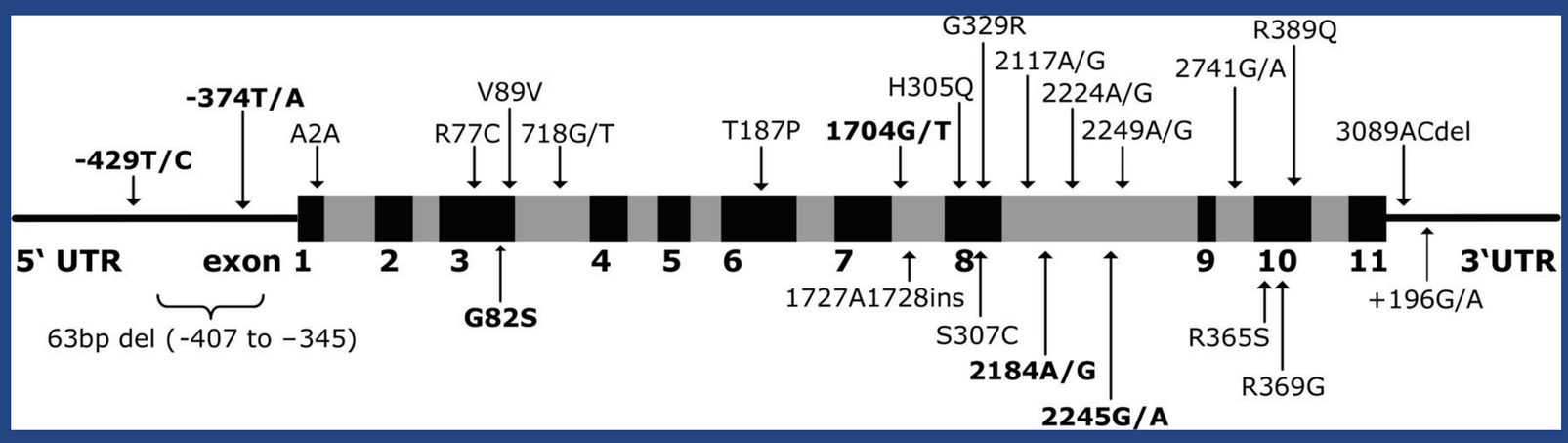


Fig. 1 – SNP map of the RAGE gene. (Kanková K et al. Nephrol. Dial. Transplant. 2005;20:1093-1102)

| Polymorphism | Allelic and genotype frequencies in each groups | | chi² - test | Hardy–Weinberg Equilibrium test |
|---|---|---|---|---|
| **GLO I A419C (%)** | Controls | A 55.5, C 44.5, AA 33.8, AC 43.5, CC 22.7 | p = 0.02 | NS |
| | ccRCC | A 41.4, C 58.6, AA 20.1, AC 42.5, CC 37.4 | | NS |
| **RAGE – 374 T/A (%)** | Controls | T 64.3, A 35.7, TT 44.8, TA 39.0, AA 16.2 | NS | NS |
| | ccRCC | T 66.6, A 33.5, TT 43.5, TA 44.9, AA 11.6 | | NS |
| **RAGE – 429 T/C (%)** | Controls | T 83.5, C 16.6, TT 70.8, TC 25.3, CC 3.9 | NS | NS |
| | ccRCC | T 79.6, C 20.4, TT 66.4, TC 26.4, CC 7.0 | | p = 0.009 |
| **RAGE G82S (557G/A) %** | Controls | G 96.4, A 3.6, GG 93.5, GA 5.8, AA 0.7 | NS | NS |
| | ccRCC | G 96.5, A 3.5, GG 93.5, GS 6.1, SS 0.4 | | NS |
| **RAGE 2184A/C (%)** | Controls | A 84.1, G15.9, AA 71.4, AG 25.3, GG 3.3 | NS | NS |
| | ccRCC | G 82.0, A 18.0, GG 68.2, AG 27.6, GG 4.2 | | NS |

Tab. 1 – Allelic and genotype frequencies of studied polymorphism for receptor glyoxalase I and RAGE in patient with ccRCC and controls

**Conclusion:** Our results clearly indicate the association of the GLO I /A419C/ polymorphism with the development of ccRCC. Fuhrmann grade 4 was associated with RAGE gene polymorphism -429T/C, -2184A/G.

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