Carlos Alberto de Carvalho Fraga, J Diabetes Metab 2014, 5:10
http://dx.doi.org/10.4172/2155-6156.S1.027

OMICS Group Conferences
Accelerating Scientific Discovery

5th World Congress on
Diabetes & Metabolism
November 03-05, 2014 Embassy Suites Las Vegas, USA

Ang-(1-7) decreases HIF-1α and migration of oral squamous cell carcinoma

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In this study, we investigated the involvement of the Ang-(1-7)/Mas axis in cell migration under hypoxic condition induced by cobaltous chloride and the underlying mechanism.

Methods and Results: We first confirmed that Ang-(1-7) decreases HIF-1α signaling in a newly developed hydroxypropyl-β-cyclodextrin (HPBCD)-based Ang-(1-7) nano-formulation in a novel transgenic rat model of inducible insulin resistance and DM2. The chronic administration of this compound prevented the marked elevation of HIF-1α in diabetic rat kidney. Next, mouse embryonic fibroblasts (MEFs) and SCC-9 cells were incubated in a well humidified incubator with 5% CO2 and 95% air at 37 °C (normoxic condictions). For hypoxic cultures, cells were incubated 150 μM CoCl2 for 24 hours and maintained in a 5% CO2 atmosphere at 37˚C. Then, we divided cells into 4 groups including control, CoCl2, Ang-(1-7) and CoCl2 + Ang-(1-7). HIF-1α protein expression and AKT phosphorylation were decreased in hypoxic cells after treatment with Ang-(1-7). Besides, Ang-(1-7) decreased SCC-9 cell migration in hypoxic condition.

Conclusions: In conclusion, our current findings suggest that Ang-(1–7) attenuates HIF-1 α protein stabilization via AKT and Mas receptor-dependent mechanism. In addition, we found that the Ang-(1–7)/Mas receptor inhibit oral cancer cell migration.

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