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In collaborazione con

Dipartimento Medicina Veterinaria Produzioni Animali

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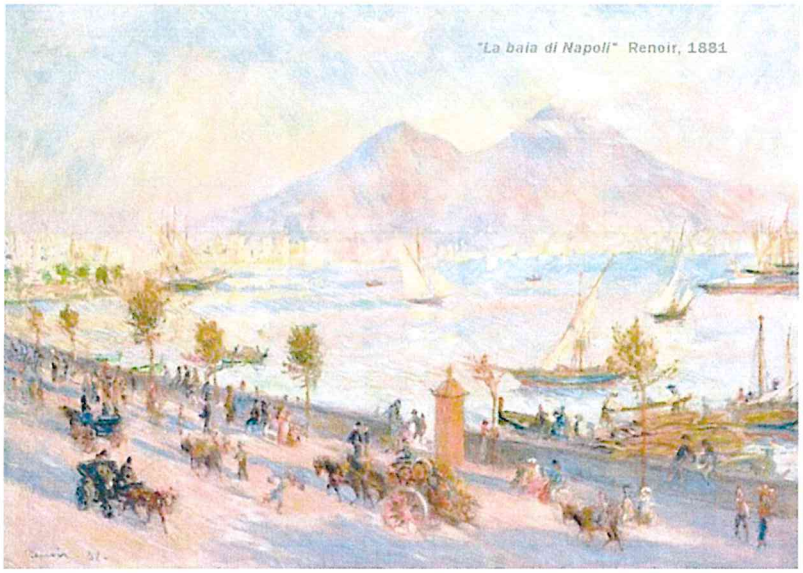

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IMPACT OF CADMIUM EXPOSURE ON SWINE ENTEROCYTES

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Cadmium (Cd) is a toxic and carcinogenic heavy metal widely distributed in the environment. The ingestion of contaminated food and drinking water is the major source of exposure to Cd and gut is the first target of interaction. However, little is known about Cd interaction with the intestinal tract (1). The aim of our study was to investigate the effects of low and high concentrations of Cd on swine enterocytes in terms of gene expression, cytotoxicity, Cd uptake, as well as of host-pathogen interaction. Swine intestinal IPEC-J2 cells were used as model. These were treated with 2 µM or 20 µM Cd solutions and incubated at 37°C in 5% CO2 for 1, 3, 6 or 24 hours. The parameters under study were described in previous studies (2-3-4). Each test was performed twice, untreated wells being used as negative control. The statistical significance of differences among the experimental groups were evaluated by one-way ANOVA or Kruskal-Wallis test. The significance threshold was set at $P< 0.05$. The ability of IPEC-J2 cells to uptake Cd was investigated first. Our data showed a significant ($P<0.001$) increase of intracellular Cd after 3 ($P<0.001$), 6 ($P<0.001$) or 24 hours ($P<0.001$) of exposure with respect to 1 hour. This was confirmed for both 2 µM ($P<0.001$) and 20 µM ($P<0.001$) Cd. The absorption of Cd was related to a significant reduction ($P< 0.0001$) of cell viability after treatment with 20 µM Cd. No effects were shown after treatment with 2 µM Cd. Concerning the modulation of gene expression, cells treated with 2 µM Cd for 1, 3, 6 or 24 hours showed a significant increase ($P<0.05$) of inflammatory gene expression (IL-6, IL-8, MYD88, NFkb1, NFkb-p65, IL-18) at all-time points, respect to untreated wells. These data are in agreement with previous studies (1) and highlight a pro-inflammatory effect of low concentrations of Cd. Treatment with 20 µM Cd caused up-regulation ($P< 0.05$) of IL-8 after 1 hour of exposure followed by a reduction of IL-8, p38, NFkb1, CD14 and STAT3 gene expression after 3 hours of treatment. At the same time, we observed up-regulation of IL-18, TNF-α, MYD88, JNK, IFN-β, BD1, BD2, TLR5 and MD2 gene expression. These effects were followed by up-regulation of Type I IFNs and IL-8 gene expression after 6 hours of exposure. 20 µM Cd caused up-regulation of IL-8, IL-1β, JNK, BD1, BD3 and BD4 and down-regulation of p38, NFkb1, MYD88, NFkb-p65 CD14, and TLR4 after 24 hours of treatment. These data support the ability of Cd to modulate inflammatory responses in swine enterocytes. Moreover, the down-regulation of inflammatory responses observed after 3 h of treatment with 20 µM of Cd, was associated with a significant ($P<0.05$) reduction of *Salmonella typhimurium* penetration into IPEC-J2 cells. In conclusion, our results indicate that exposure to Cd may modify the basal level of cytokine expression, thereby influencing different compartments of the innate immune response.

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