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Influence of membrane fatty acid composition on cell viability and lipid peroxidation in a cell model (AR42J) of cerulein-induced acute pancreatitis

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Oxidative stress is a major pathogenic factor in both human and experimental acute pancreatitis[1]. Cerulein produces in isolated pancreatic acinar cells large amounts of reactive oxygen species[2], which can then attack the pancreatic membranes directly and also can act as chemoattractants for inflammatory cells[1]. We aimed to determine whether modification of membrane fatty acid profile of pancreatic AR42J cells influences cell viability and lipid peroxidation after cerulein treatment.

Membrane fatty acid changes were evoked by culturing AR42J cells for 72 h in medium enriched with 18:1*n*-9 (50 μM, AR42J-O) or *n*–3 PUFA (15 μM 20:5*n*-3 + 10 μM 22:6*n*-3, AR42J-n3). Cells cultured in standard medium were used as a control (AR42J-C). The detailed procedure is described elsewhere[3]. Cells grown in this way were then treated with cerulein for 24 h. Cell viability was determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Lipid peroxidation was assessed by measurement of 8-isoprostane in conditioned media using a commercial enzyme immunoassay (Cayman Chemical, Ann Arbor, Michigan, USA). AR42J crude membranes became enriched in those specific fatty acids added to the medium (Table 1). Cerulein decreased cell viability in all the three groups. For a given concentration, cell viability reached minimum values in AR42J-n3 (Fig. 1). Cerulein increased 8-isoprostane concentration only in AR42J-n3 cells. Comparison between the groups (Fig. 2) shows higher peroxide levels in AR42J-n3 cells for both 10^{-8} and 10^{-7} M.

Table 1. Percentage of total fatty acid content (n = 10–22). Values with different superscript letters are different at P < 0.05 (one-way ANOVA). UI: unsaturation index

	AR42J-C		AR42J-O		AR42J-n3	
	Mean	SE	Mean	SE	Mean	SE
18:1n – 9	25.69[a]	0.41	32.40[b]	1.11	19.84[c]	0.53
20:5n – 3	0.58[a]	0.02	0.36[a]	0.02	4.37[b]	0.36
22:6n – 3	1.87[a]	0.10	1.08[b]	0.06	7.08c	0.11
SFA	53.06[a]	0.40	49.13[b]	0.95	52.12[a]	0.75
MUFA	30.02[a]	0.36	36.90[b]	0.99	23.58[c]	0.47
n – 6 PUFA	8.57[a]	0.26	5.05[b]	0.13	8.06[a]	0.21
n – 3 PUFA	6.28[a]	0.24	6.55[a]	0.32	14.11[b]	0.61
UI	1.55[a]	0.03	1.54[a]	0.04	2.30[b]	0.08

Our results suggest a modulatory role for membrane lipid composition in cell viability and lipid peroxidation in pancreatic acinar cells exposed to aetiologic agents for pancreatitis. This may have pathophysiologic relevance considering that habitual intake of specific dietary fats influences the fatty acid profile of pancreatic membranes *in vivo*[4].

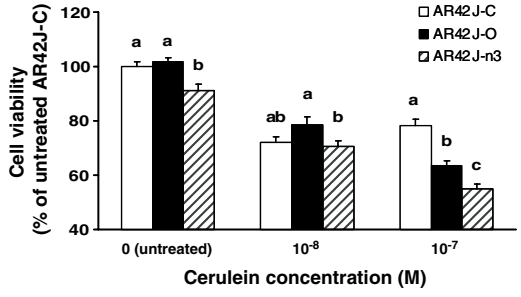

Fig. 1. Means with their standard errors (n = 28–56). For a given cerulein concentration, values with different letters are different at $P < 0.05$ (one-way ANOVA).

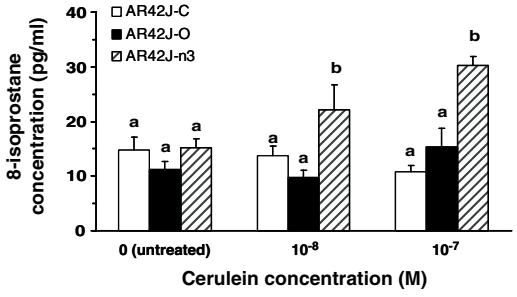

Fig. 2. Means with their standard errors (n = 5–6). For a given cerulein concentration, values with different letters are different at $P < 0.05$ (one-way ANOVA).

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