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### CARDIOPATIA ISCHEMICA

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ISCHEMIA, STUDI SPERIMENTALI (*ISCHEMIA / ACS / INFARTO*)ISCHEMIA E PROTEZIONE (*SCIENZA DI BASE*)FISIOLOGIA INTEGRATIVA E MECCANISMI DI CONTROLLO (*SCIENZA DI BASE*)

### PASTA ENRICHED WITH BARLEY(1-3)BETA-D-GLUCAN INCREASES MYOCARDIAL PARKIN EXPRESSION AND PREVENTS CARDIAC ISCHEMIA/REPERFUSION INJURY IN MICE

Valentina Casieri (a), Marco Matteucci (a), Gaia Papini (a), Silverio Sbrana (c), Michele Torelli (d), Vincenzo Lionetti (a, b)

(a) LABORATORY OF MEDICAL SCIENCE, INSTITUTE OF LIFE SCIENCES, SCUOLA SUPERIORE SANT'ANNA, PISA, ITALY; (b) FONDAZIONE TOSCANA "GABRIELE MONASTERIO", PISA, ITALY; (c) INSTITUTE OF CLINICAL PHYSIOLOGY, NATIONAL COUNCIL OF RESEARCH, PISA, ITALY; (d) PASTIFICIO ATTILIO MATROMAURO GRANORO S.R.L., CORATO, ITALY

**Introduction:** Parkin, an E3 ubiquitin ligase, is required for cardioprotective effects of ischemic preconditioning by triggering mitophagy. However, the noninvasive induction of myocardial parkin level is a desirable achievement. (1-3)  $\beta$ -D-glucan, a water-soluble polysaccharide, protects against cardiac ischemia/reperfusion (I/R) injury, yet mechanisms are still unknown.

**Hypothesis:** Dietary intake of pasta enriched with 3% w/v barley (1-3)  $\beta$ -D-glucans upregulates the expression of parkin in cardiomyocytes and increases cell resistance to I/R microenvironment.

**Methods:** Adult male C57BL/6 mice were fed for 5 weeks with a low-fat diet supplemented with pasta enriched with barley (1-3)  $\beta$ -D-glucan (3g/100mg) ( $\beta$ -D-glucan, n=15) or regular pasta (control, n=15). Food and caloric intake, glucose tolerance test and cardiac function were weekly assessed. At fifth week of diet, each group underwent to 30 min of cardiac ischemia and 60 min of reperfusion. Infarct size/area at risk was assessed at the end of cardiac reperfusion. Myocardial expression of parkin and p53, a parkin inhibitor, were measured by western blot. Cardiac anion superoxide (O<sub>2</sub><sup>-</sup>) load was detected by dihydroethidium staining. To evaluate the impact of  $\beta$ -D-glucan on mitophagy, we further examined the parkin level and mitochondria JC1 staining green in  $\beta$ -D-glucan-treated HL1 cardiomyocytes exposed to acute oxidative stress (100uM H<sub>2</sub>O<sub>2</sub>).

**Results:** Food and caloric intake, plasma glucose level and cardiac function were similar in both groups. Dietary supplementation with functional pasta increased myocardial parkin level by 85±2% (P<0.00001) without altering p53 protein expression. At the end of cardiac I/R, survival of  $\beta$ -D-glucan mice was significantly increased by 50±2% compared to control. Infarct size/area at risk was reduced by 62±5% (P<0.001) in  $\beta$ -D-glucan mice in the presence of reduced myocardial O<sub>2</sub><sup>-</sup> load (P<0.0001). In vitro, JC1 staining green was increased in  $\beta$ -D-glucan-treated HL1 (P<0.001), which have shown higher parkin level and resistance to oxidative burst.

**Conclusions:** Long-term dietary intake of pasta enriched with 3% w/v barley  $\beta$ -D-glucan increased cell survival to I/R microenvironment and reduced infarct size through increasing parkin-dependent mitophagy in cardiomyocytes.