MYELOID CELL 11β-HSD1 REGULATES THE INFLAMMATORY RESPONSE DURING MYOCARDIAL INFARCT HEALING AND PROTECTS THE HEART FROM DETRIMENTAL REMODELLING AFTER IRRADIATION AND BONE MARROW TRANSFER

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11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) is responsible for intracellular regeneration of glucocorticoids. 11β-HSD1-deficient mice exhibit enhanced angiogenesis, inflammatory cell recruitment and heart function after myocardial infarction (MI). This study aimed to determine the role of myeloid cell 11β-HSD1 on the response to MI, induced by coronary artery ligation.

Irradiated wild-type (WT) mice received 10 million nucleated WT bone marrow cells or cells from 11β-HSD1−/− mice. Successful reconstitution was confirmed by flow cytometry in blood, spleen and thymus.

High-resolution ultrasound prior to MI revealed reduced ejection fraction (EF) in mice that received 11β-HSD1−/− (43.5±3.2%) vs WT bone marrow (66.4±1.2%; p<0.01). LV end-diastolic area was also increased (p<0.05). Seven days after MI, EF decreased in mice that received WT cells (26.4±6.3%; p<0.01), but was not further reduced in those with 11β-HSD1−/− cells (36.61±3.6%; ns).

Significant fibrosis (picrosirius red) was evident in ventricles of mice that had received 11β-HSD1−/− (2.1±0.4% LV) vs WT bone marrow (0.3±0.4% LV). In the healing infarct zone, there was a greater representation of alternatively activated (YM-1+ve) cells amongst recruited macrophages in mice receiving 11β-HSD1−/− bone marrow.

These data demonstrate that myeloid cell 11β-HSD1 may be key to determination of recruited cell phenotype early after MI. Further studies are required to investigate whether similar modification of inflammation underlies the unexpected ventricular remodelling and loss of function that follows exposure to irradiation.


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