**miR-125a, miR-139 and miR-324 contribute to Urocortin protection against myocardial ischemia-reperfusion injury**

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| miRNA | Predicted gene target | Full gene name | sequence ref |
|---|---|---|---|
| miR-125a-3p | Mtfr1 | mitochondrial fission regulator 1 | NM_001100977.1 |
| | Igf2 | insulin-like growth factor 2 | NM_001190162.1 |
| | Map3k12 | mitogen activated protein kinase kinase kinase 12 | NM_013055.1 |
| | Brca1 | breast cancer 1 | NM_012514.1 |
| | Xbp1 | X-box binding protein 1 | NM_001004210.2 |
| | Map2k7 | mitogen activated protein kinase kinase 7 | NM_001025425.1 |
| | Cpt2 | carnitine palmitoyltransferase 2 | NM_012930.1 |
| | Taz | tafazzin | NM_001025748.1 |
| | Rgs4 | regulator of G-protein signaling 4 | NM_017214.1 |
| | Smad4 | SMAD family member 4 | NM_019275.2 |
| | Nrg1 | neuregulin 1 | NM_001271130.1 |
| miR-139-3p | Igf1r | insulin-like growth factor 1 receptor | NM_052807.2 |
| | FoxO1 | forkhead box O1 | NM_001191846.2 |
| | CxcR4 | chemokine (C-X-C motif) receptor 4 | NM_022205.3 |
| | Pde4A | phosphodiesterase 4A | NM_013101.3 |
| | Gnb1 | guanine nucleotide binding protein, beta polypeptide 1 | NM_030987.2 |
| | Col5a2 | collagen, type V, alpha 2 | NM_053488.1 |
| | Camta2 | calmodulin binding transcription activator 2 | NM_001105801.2 |
| miR-324-3p | Crebbp | CREB binding protein | NM_133381.3 |
| | STAT2 | signal transducer and activator of transcription 2 | NM_001011905.1 |
| | Bcl2l11 (Bim) | BCL2-like 11 | NM_022612.1 |
| | Dnajb6 | DnaJ (Hsp40) homolog, subfamily B, member 6 | NM_001013209.1 |
| | Nfat5 | nuclear factor of activated T-cells 5 | NM_001107425.1 |
| | Dag1 | dystroglycan 1 (dystrophin-associated glycoprotein 1) | NM_053697.1 |
| | Casq1 | calsequestrin 1 | NM_001159594.1 |

**Online Table 1. List of target genes for miR-125a-3p, miR-139-3p, and miR-324-3p.**
List of target genes obtained by bioinformatics analysis using PicTar, TargetScan, and miRBase softwares.

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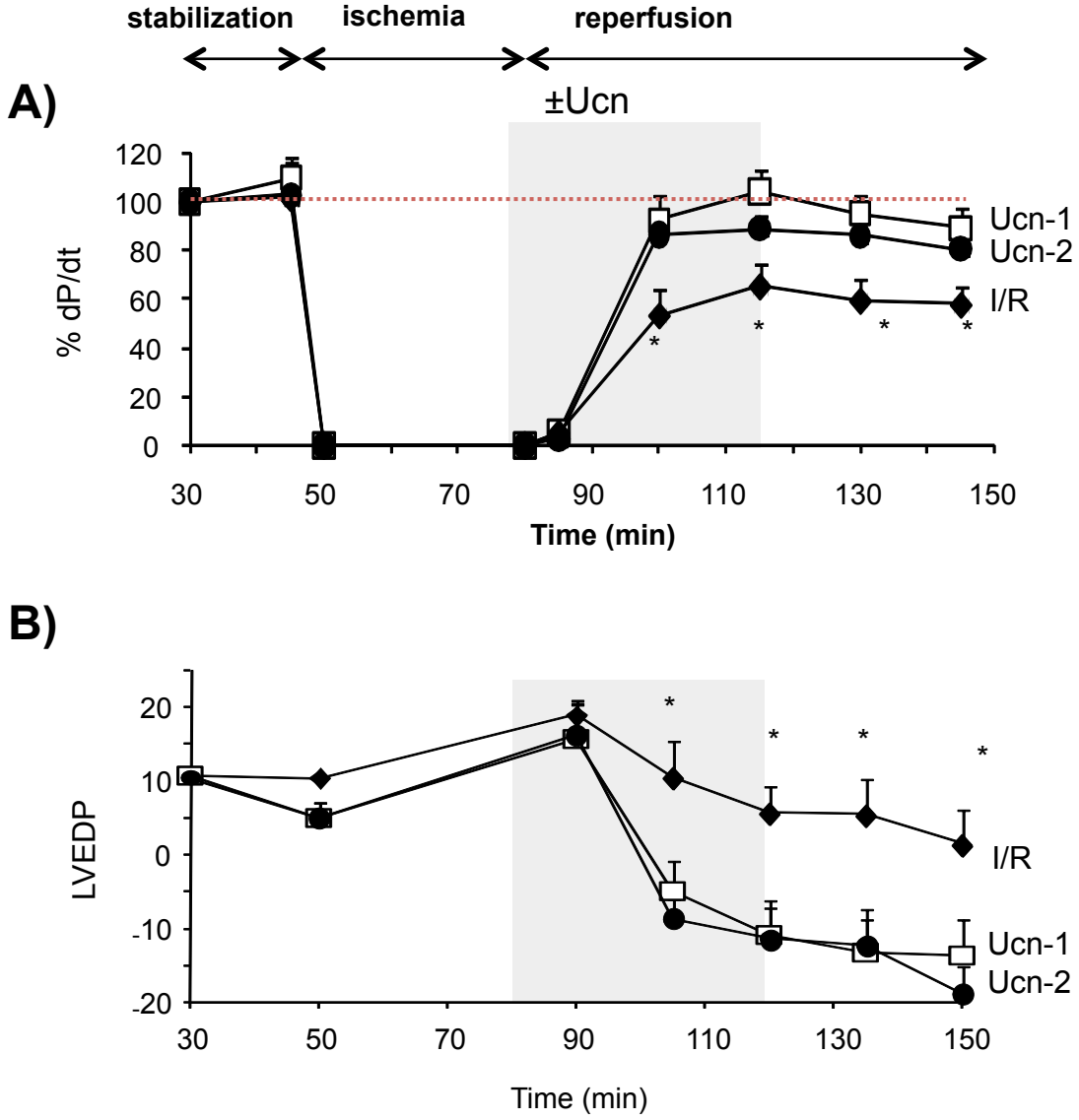


**Online Figure 1. Comparative effects of Urocortin-1 and Urocortin-2 in Langendorff-perfused rats hearts**

A) Graph shows summary data of the contractility expressed as +dP/dt (%) in hearts subjected to ischemia/reperfusion protocol (I/R, full diamond, n = 6), in hearts treated with 10 nM Ucn-1 (open square, n = 6); and in heart treated with Ucn-2 (full circle, n = 6). Ucn-1 or Ucn-2 were applied 3 minutes before ischemia ends, and it continuous during the first 30 minutes in reperfusion as indicated by area in grey. B) Shows summary data of the left ventricular end diastolic pressure (LVEDP, mmHg) in the same conditions as in "A". "*" indicates significance at $p<0.05$ of I/R vs Ucn-1 or Ucn-2.

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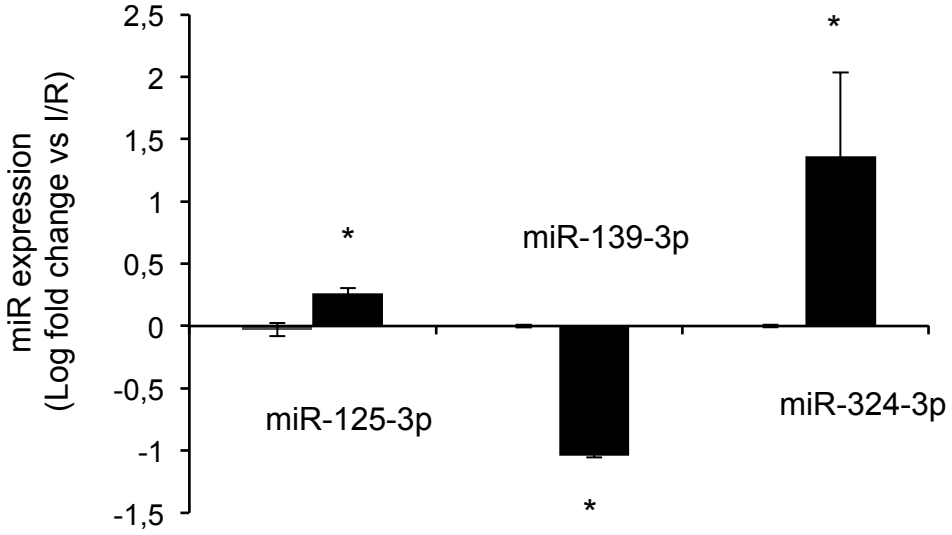


**Online Figure 2. Urocortin-1 regulates the expression of miR-125-3p, miR-139-3p and miR-324-3p in neonatal ventricular cardiac myocyte.**

Graph shows the expression of miR-125, miR-139 and miR-324 in cardiac myocyte undergoing the protocol of I/R and treated with Ucn-1 (10 nM) in reperfusion. Values are shown in logarithmic scale and are means ± S.E.M, (n = 3 independent cells preparation). "*" indicates significance at $p<0.05$.

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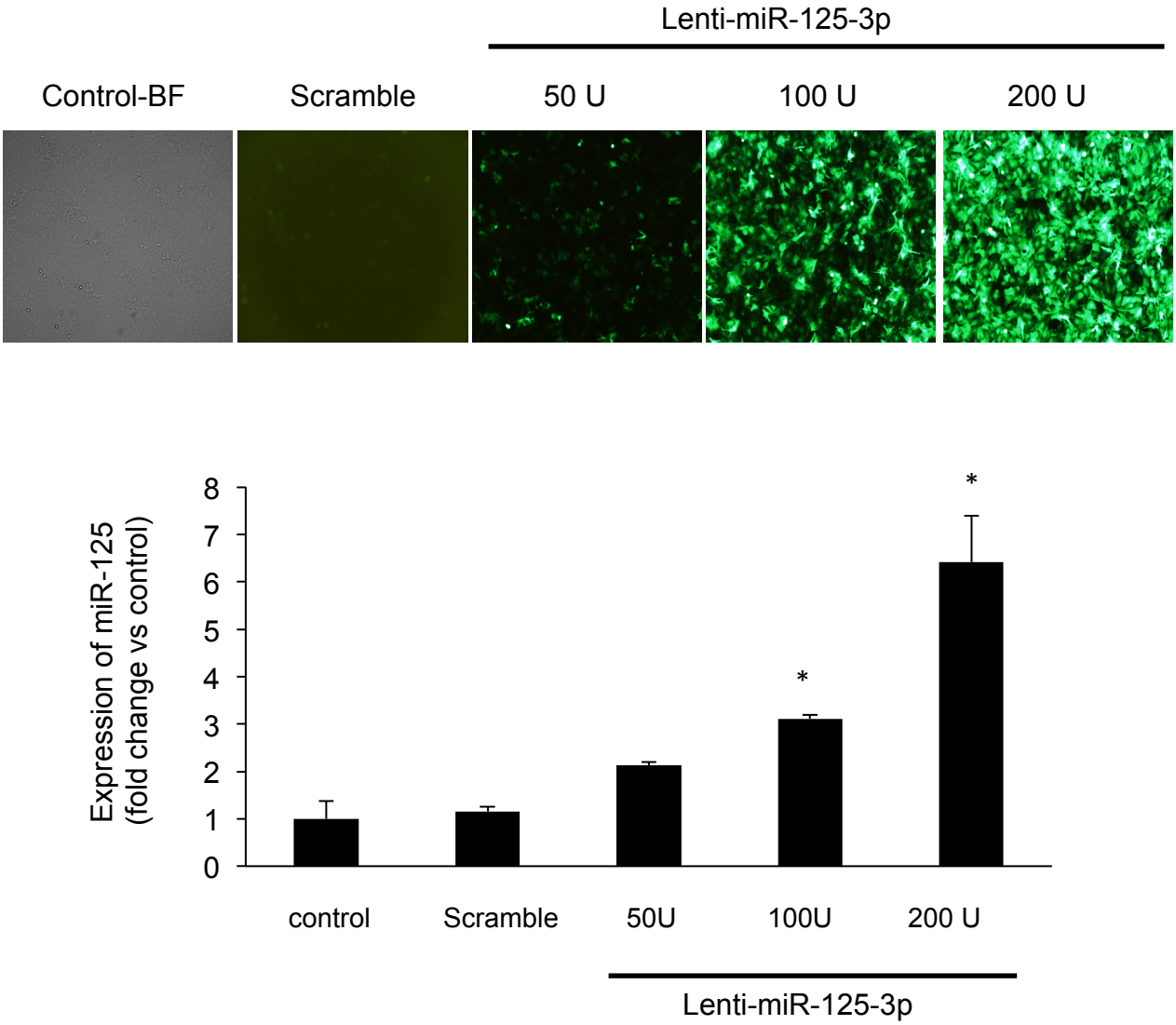


**Online Figure 3. Experiments showing the efficiency of cardiac cell transfection with lentivirus.**

A) Images of rat neonatal cardiomyocyte in the following condtions: control non transfected cells; cells transfected with lentivirus expressing scrmable miRNA; cells transfected with increasing doses of lentivirus overexpressing miR-125-3p.

B) Graph showing the expression of miR-125-3p noemalized to control value examined by q-RT-PCR. . Values aree means ± S.E.M, (n =). "*" indicates significance at $p<0.05$ vs control.