Mitophagy regulates macrophage phenotype in diabetic nephropathy rats

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Background

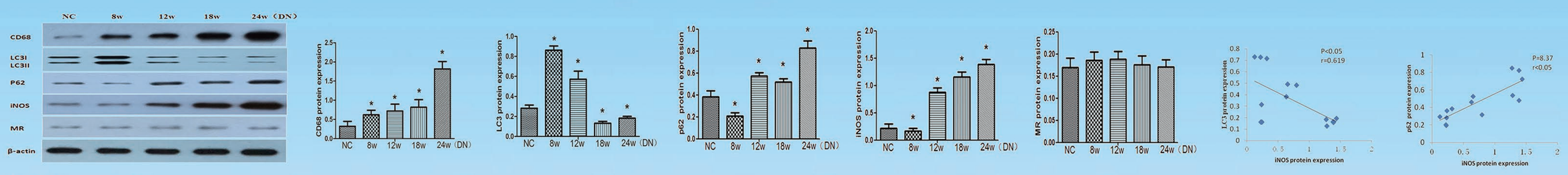
Imbalance of M1/M2 macrophages phenotype activation is a key point in diabetic nephropathy (DN). Macrophages mainly exhibit M1 phenotype, whcih contribute to the inflammation and fibrosis in DN. Studies indicate that autophage plays an important role in M1/M2 activation. However, the effect of mitophage on M1/M2 macrophage phenotype transformation in DN is unknown. The aim of this study is to explore the role of mitophage on macrophage polarization in DN.

Methods

In vivo, DN model rats were established by intraperitoneal injection with streptozocin (STZ). Rats were sacrificed respectively at 8w、12w、18w、24w for histological and molecular analysis. In vitro, RAW264.7 cells were cultured with 30mM glucose in a time- (0h, 3h, 6h, 9h, 12h, 24h, 36h) dependent manner with or without mitophage inhibitor(3-MA) and activator (rapamycin) intervention. Mitophagy-related proteins expression of LC3, Beclin-1, p62, VDAC, iNOS (phenotypic macrophages M1 marker) and MR (M2 marker) were detected by immunofluorescence and Western Blot.

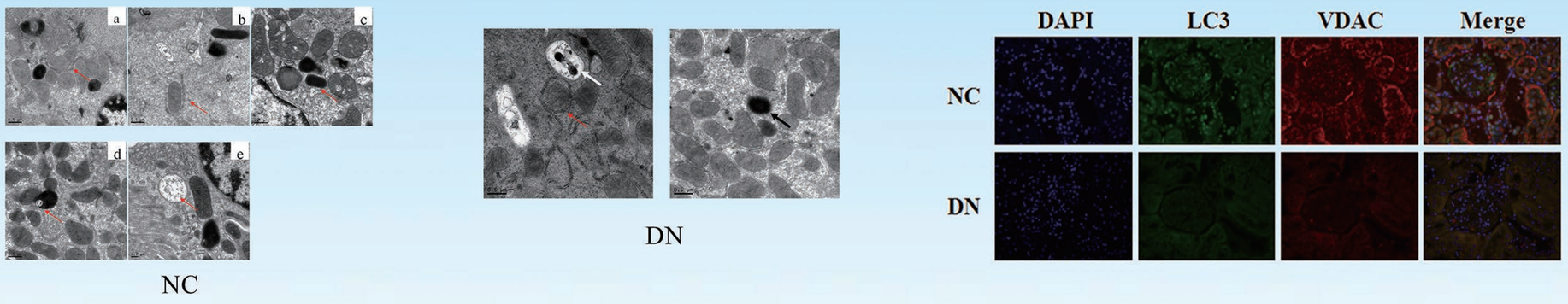
Results

1. A novel link between autophagy and macrophage M1 phenotype in DN rats.



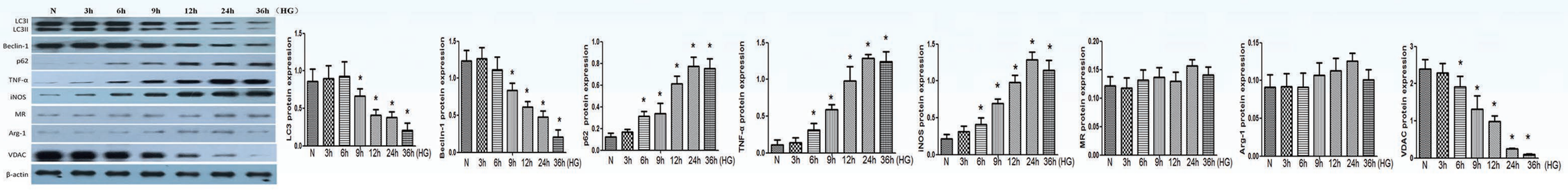
*P<0.05 vs. control group.

2. Mitochondrial morphology changes and mitopagy in DN rats renal tissue.



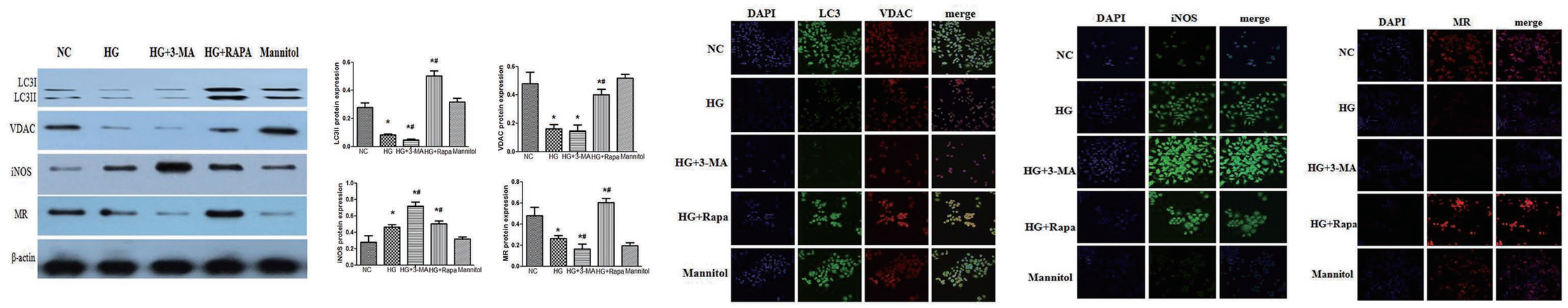
a:formation and extension of isolating membrane, b:autophagosomes formation, c:lysosome chemotaxis, d:fusion of autophagosomes with lysosomes, e: and degradation in the autolysosome.

3. RAW264.7 macrophages switched to M1 phenotype with mitophagy downregulated under high glucose conditions.



*P<0.05 vs. control group.

4. Regulation of mitophagy changes RAW264.7 macrophage M1/M2 phenotype in high glucose condition



*P<0.05 vs. control group. #P<0.05 vs. HG group.

Conclusion

Mitophage participates in the regulation of M1/M2 macrophage phenotype in diabetic nephropathy.

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