Association of Elevated Urinary miR-126, miR-155 and miR-29b with Diabetic Kidney Disease

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Introduction

Diabetes Mellitus affects 3.8 million people in the UK

Approx. 40% diabetic patients go on to develop diabetic kidney disease (DKD) the incidence of which is increasing globally

Stages of Chronic Kidney Disease (KIDOQI)*

Stage	Description	GFR (ml/min/1.73m²)
1	Kidney damage with normal or ↑GFR	≥ 90
2	Kidney damage with mild ↓GFR	60 - 89
3	Moderate ↓GFR	30 - 59
4	Severe ↓GFR	15 – 29
5	Kidney failure	< 15 (or dialysis)
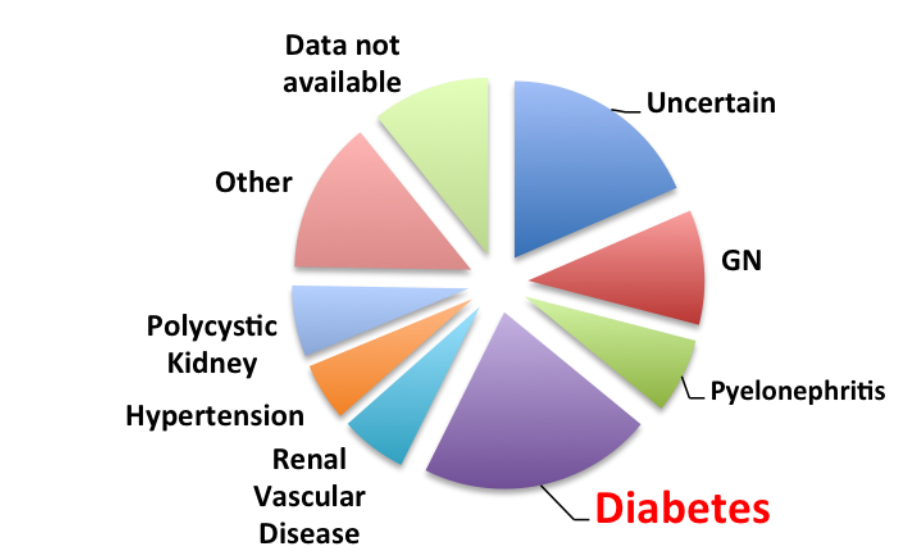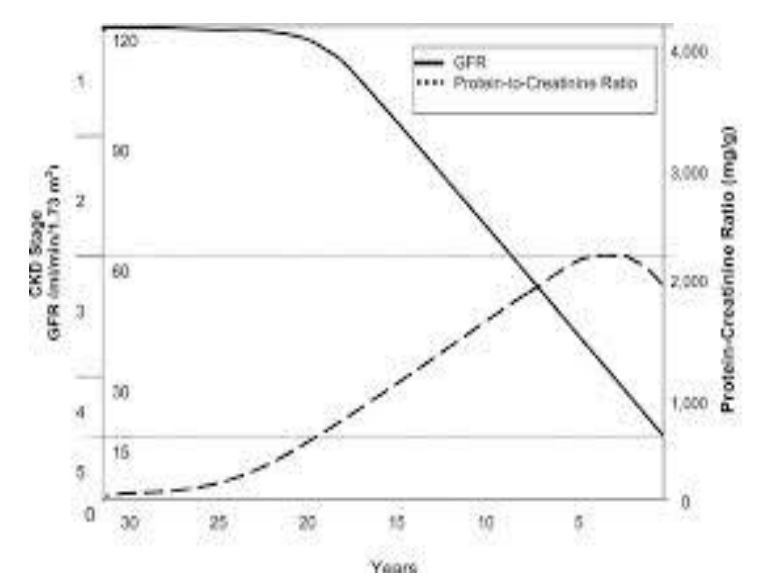
The predictive value of current non-invasive prognostic indicators for chronic kidney disease, such as urine protein quantification and declining eGFR is limited
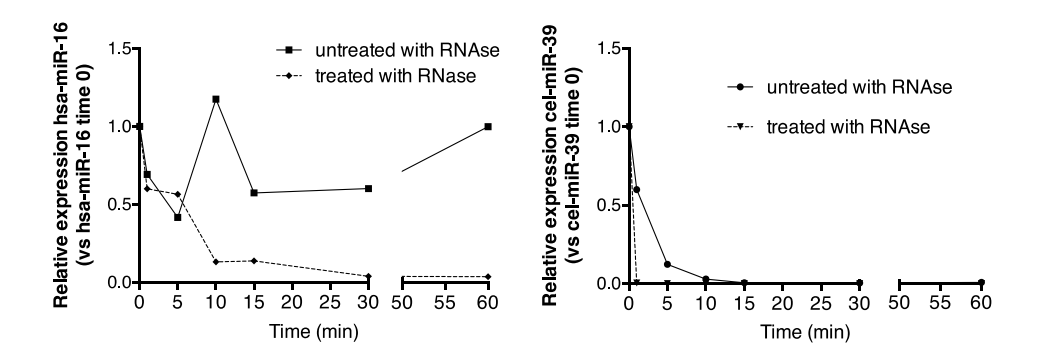
UK Renal Registry 2008

What is a microRNA

Short ssRNA molecules

Sequence-specific

Regulate expression of approx. 60% of all human protein coding genes

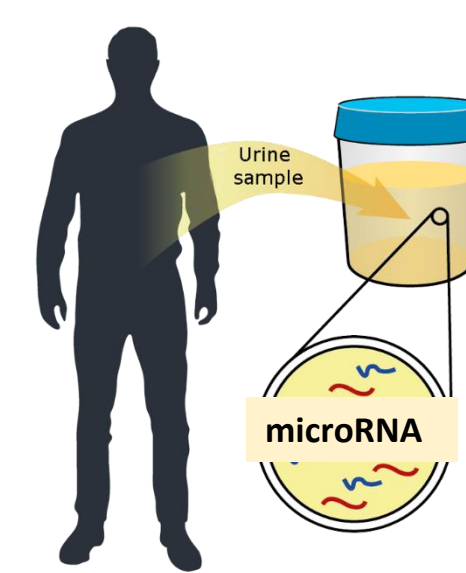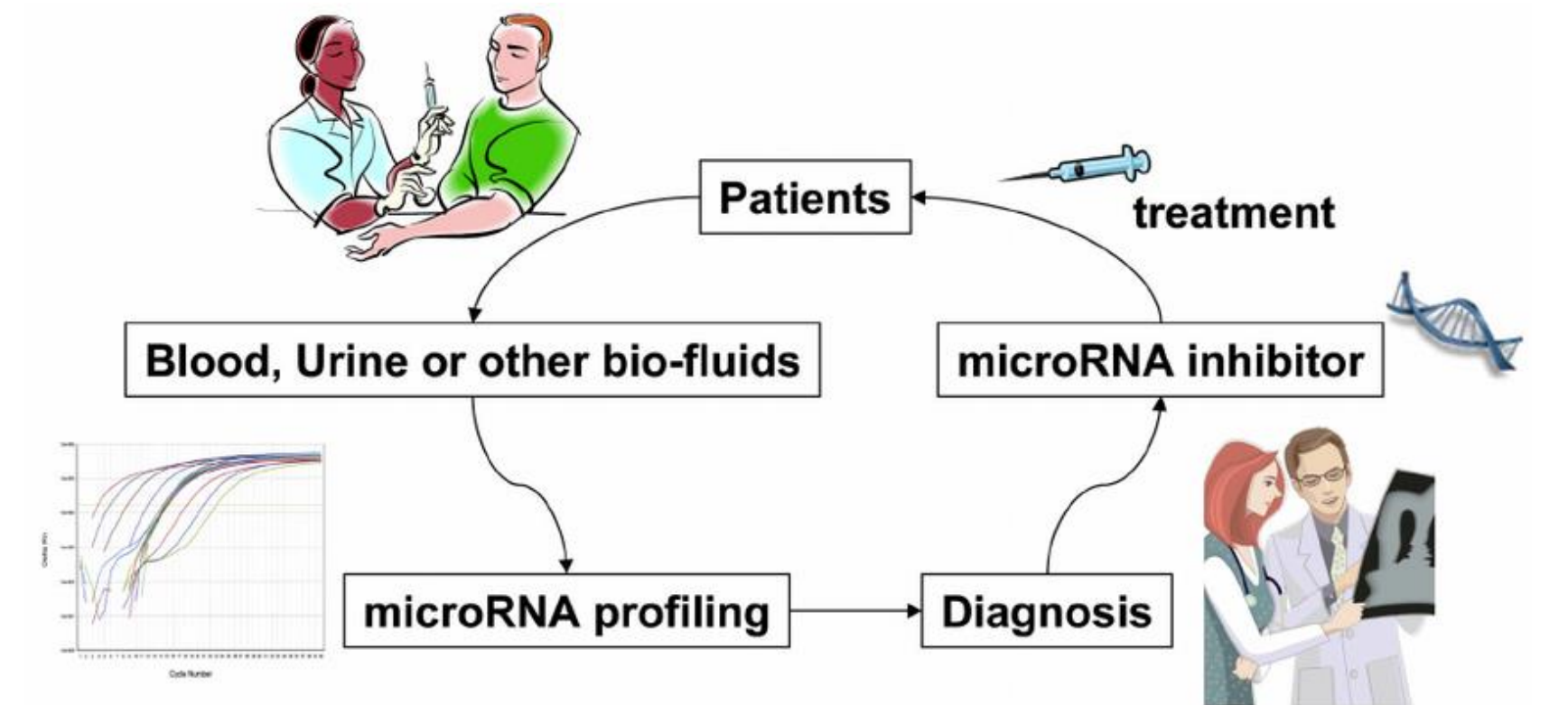In pursuit of the elusive miRNA...

Readily detectable

Relative expression of endogenous miR-16 and exogenous cel-miR-39 in urine samples following RNase A treatment for 1 h

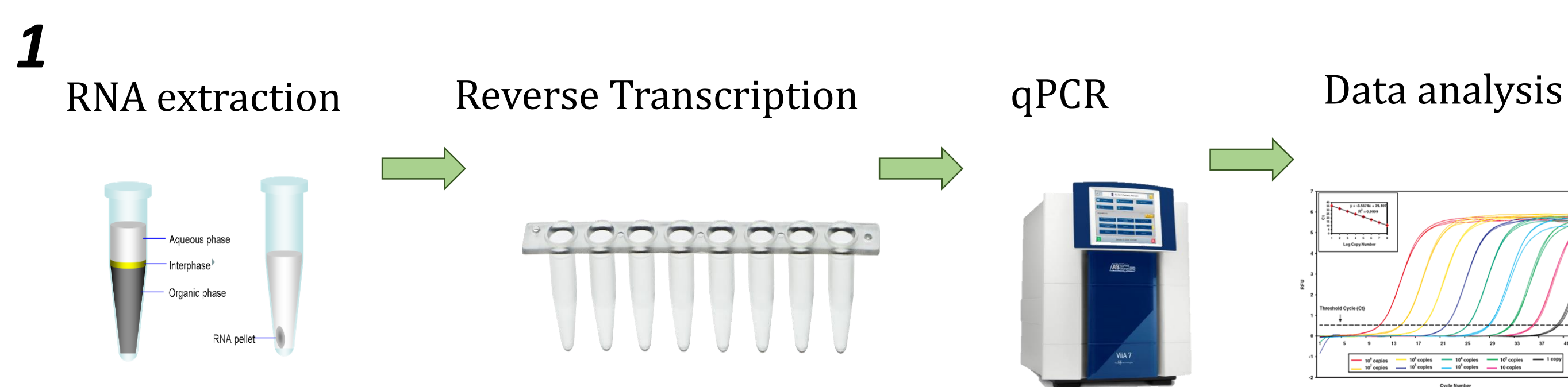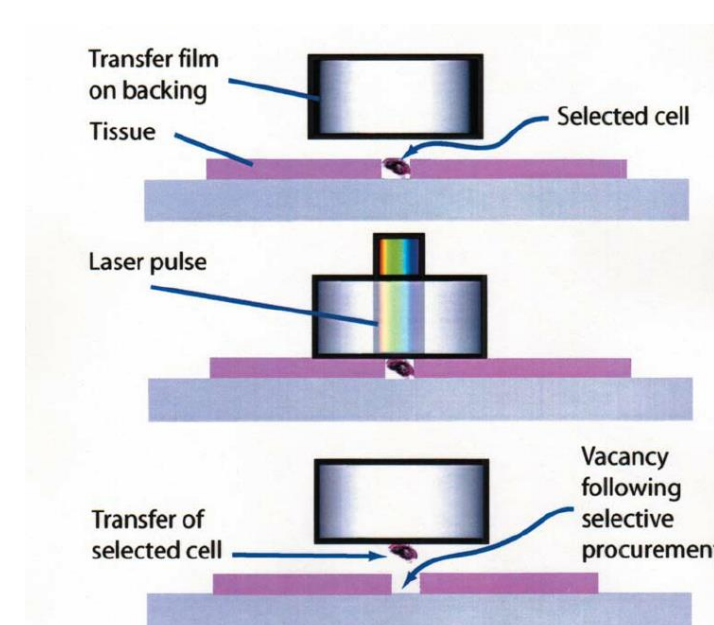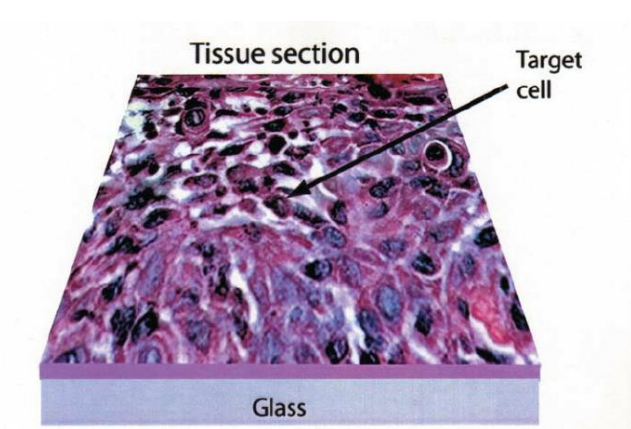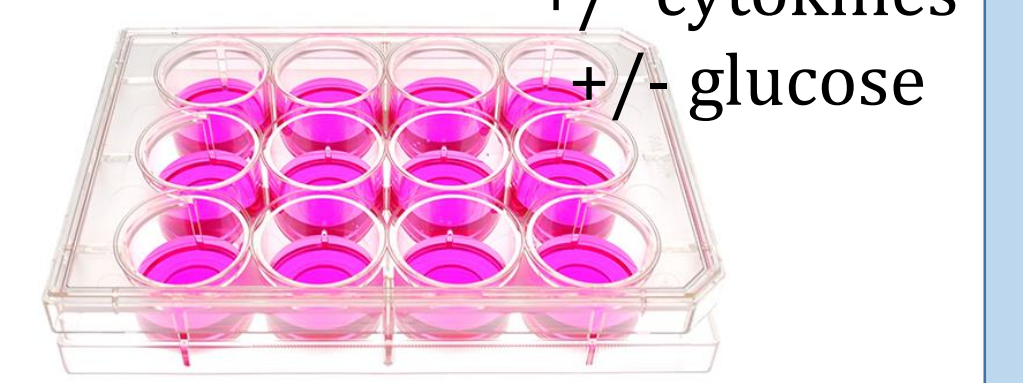### Non-invasive

Translational medicine

Methods

1

RNA extraction → Reverse Transcription → qPCR → Data analysis

2 Laser Capture microdissection (LCM)
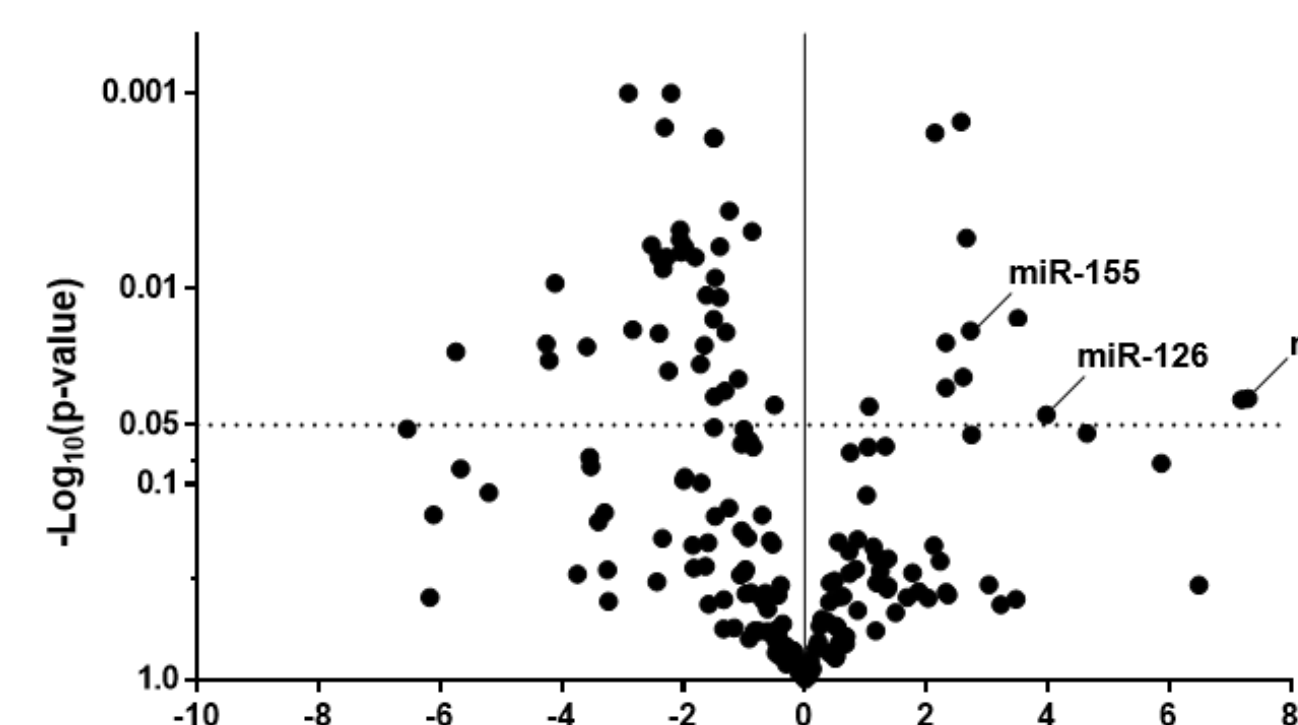
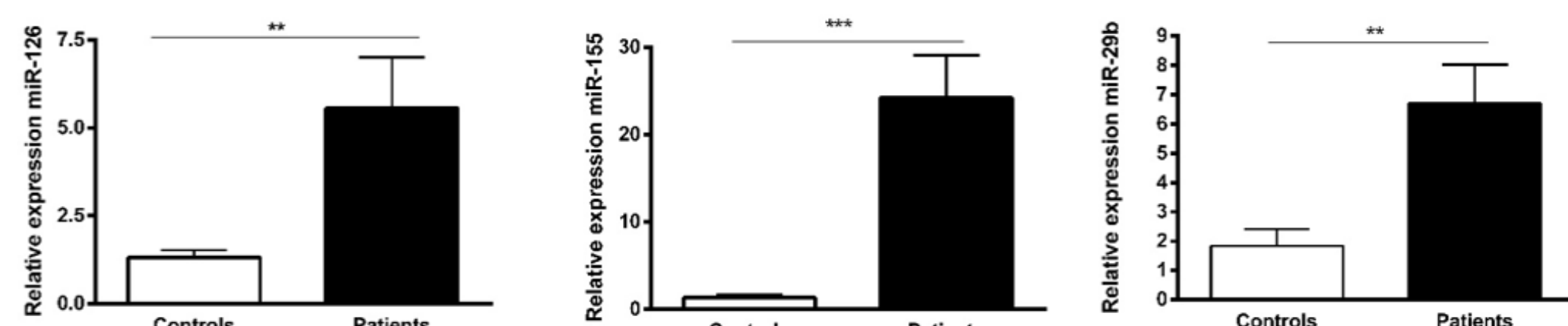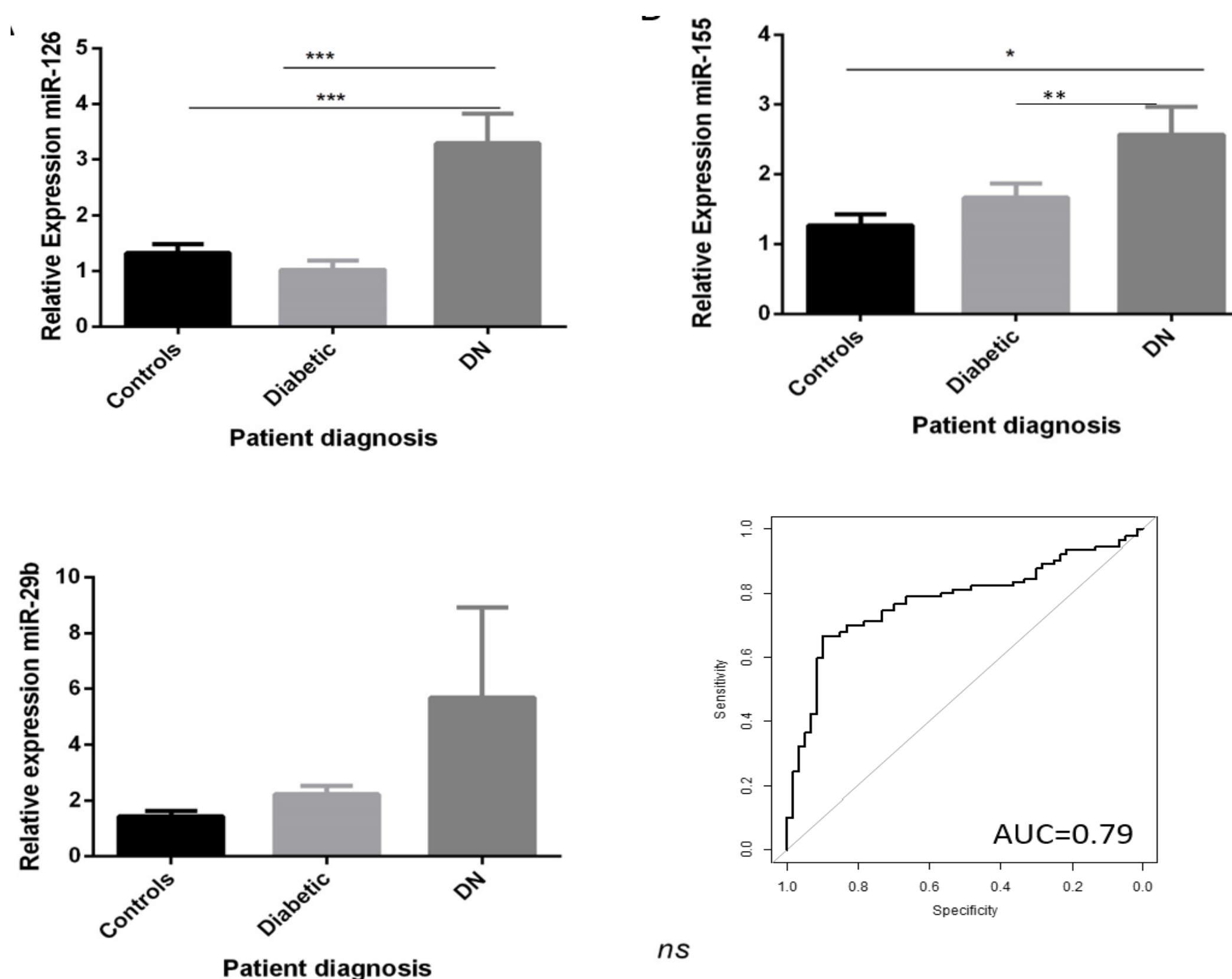**3** *In vitro* model   +/- cytokines +/- glucose

Results

Biomarker candidates

Volcano plot: analysis of 4 pooled urine samples from 5 DKD (n = 20) and 4 pooled urine samples from 5 controls (n = 20)
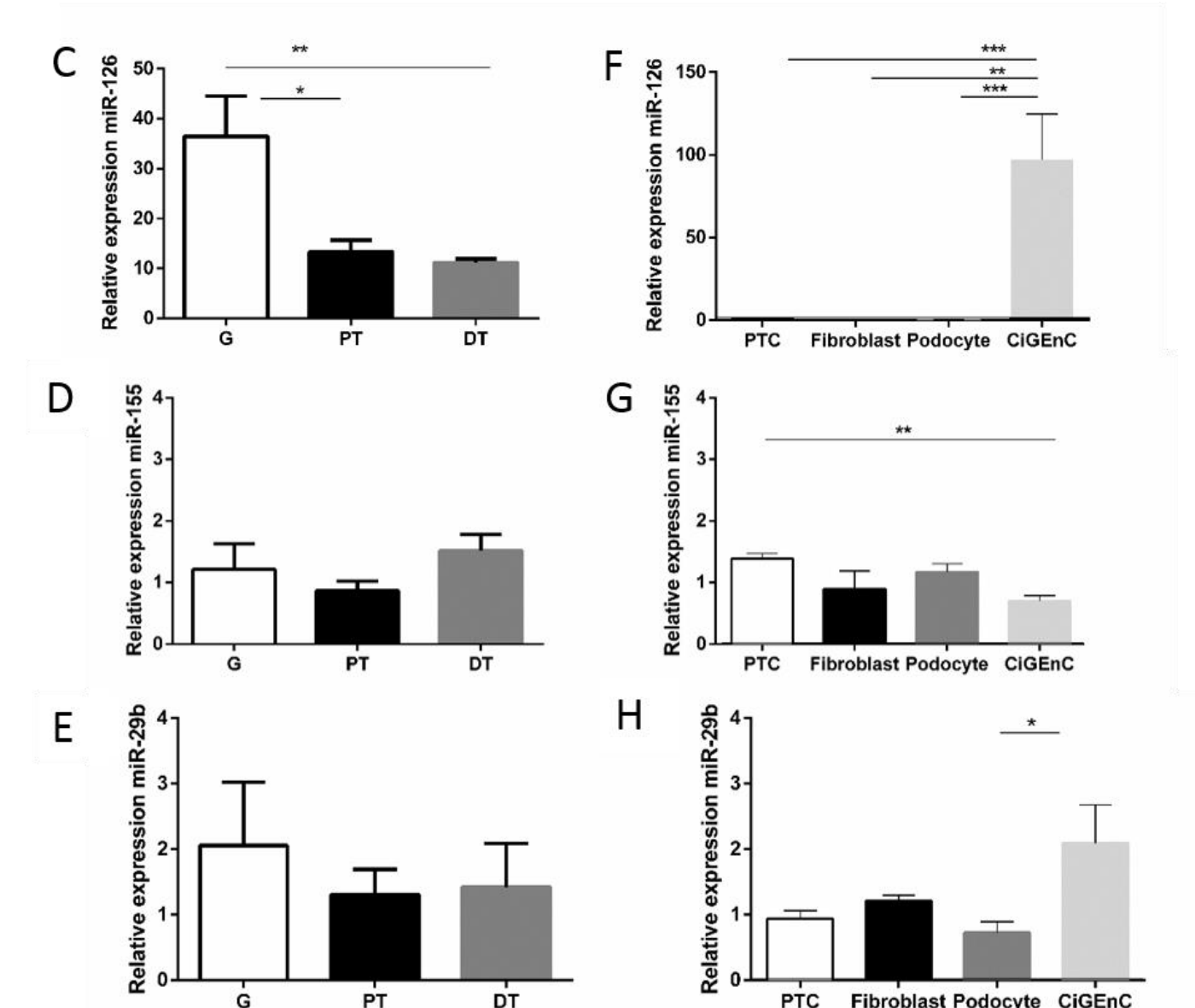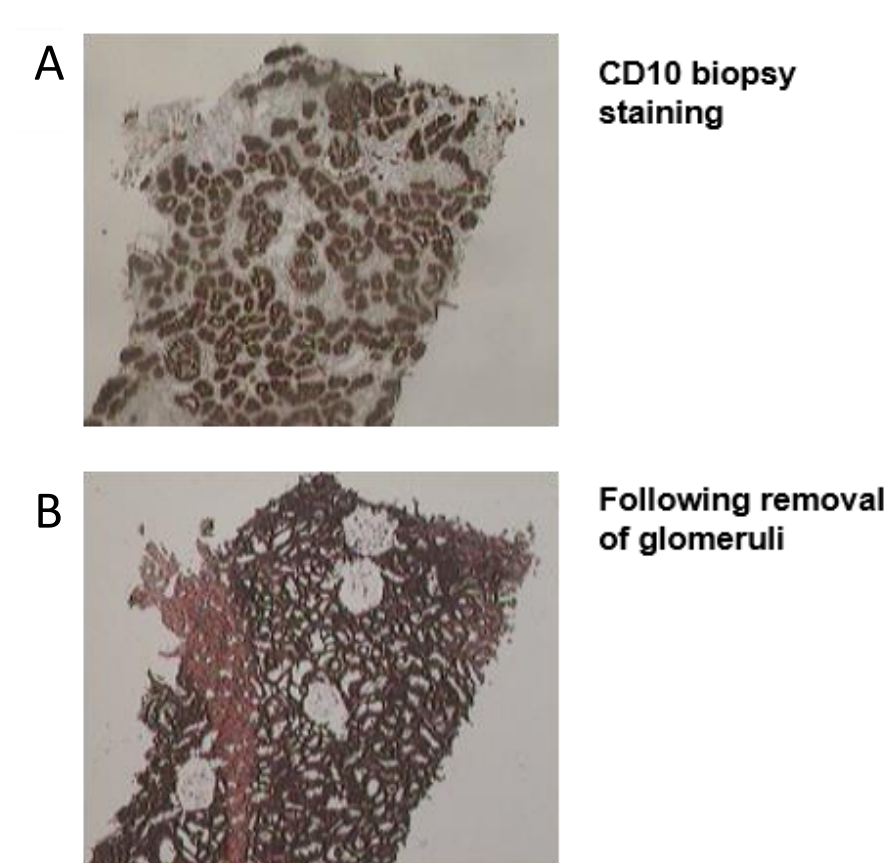

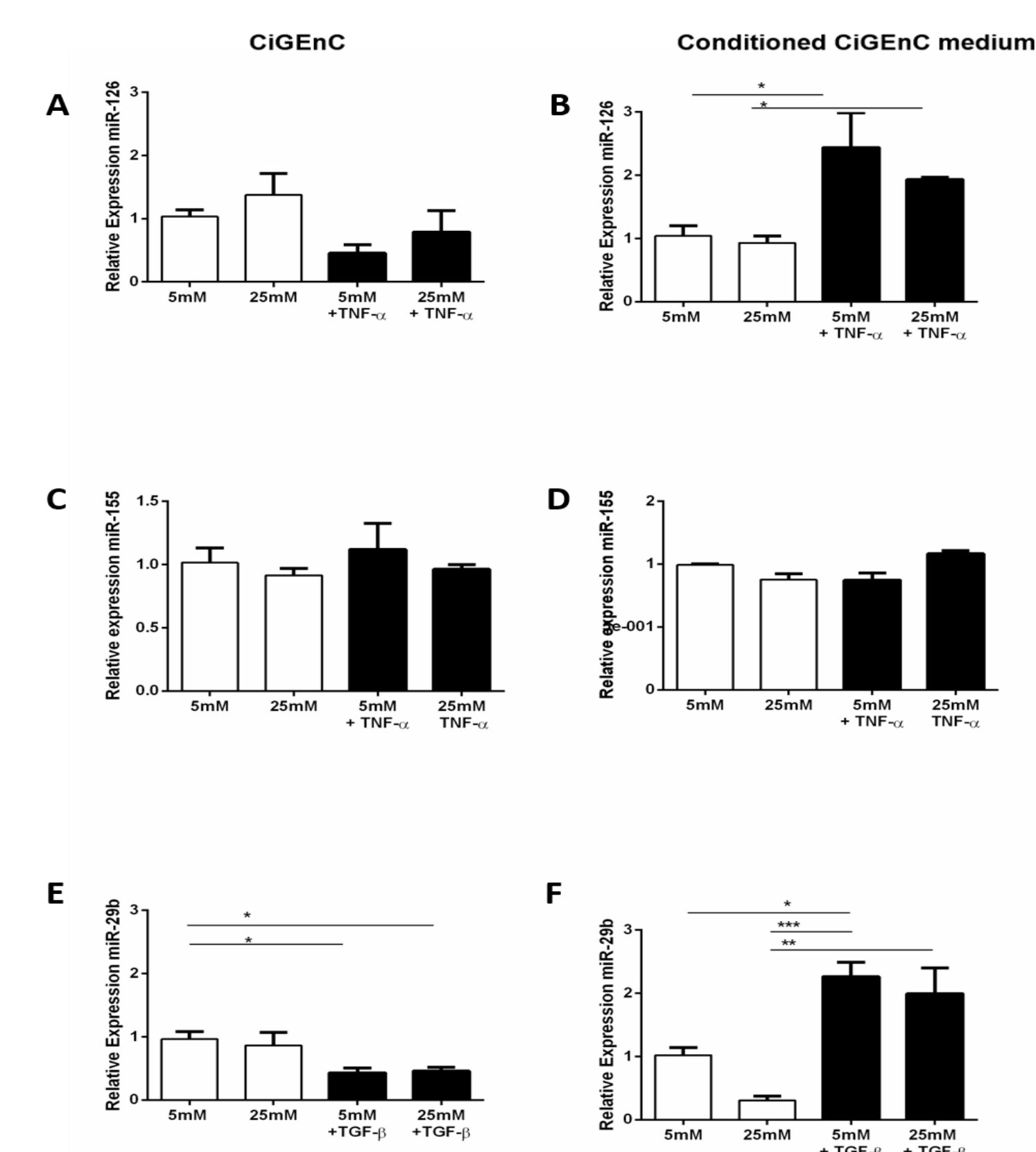Individual RT-qPCR analyses of miRs in DKD vs controls

AUC=0.79

ns

Validation: Detection of selected microRNAs in healthy, diabetic DKD independent cohorts (n=151).

MicroRNA mechanisms

A   CD10 biopsy staining

B   Following removal of glomeruli

Localization of miRNA expression by laser capture microdissection (LCM) and *in vitro models*

MiRNA expression in glomerular endothelial cells (CiGenC) and CiGenC growth media under diabetic conditions+/-cytokines, showing the release of miR-126 and 29b into the conditioned medium in response to cytokines

Conclusions

MicroRNAs show great promise as potential predictive biomarkers in CKD

Our targets show protective properties being released from the glomerulus under disease conditions *in vitro*

Acknowledgements