

# Glomerular extracellular matrix protein changes in IgA nephropathy

Flavia Teodora Ioana Paunas<sup>1</sup>, Kenneth Finne<sup>2</sup>, Sabine Leh<sup>2,3</sup>, Hans-Peter Marti<sup>1,2</sup>, Bjørn Egil Vikse<sup>1,2,4</sup>

<sup>1</sup> Department of Medicine, Haugesund Hospital, Haugesund, Norway, <sup>2</sup> Department of Clinical Medicine, University of Bergen, Bergen, Norway, <sup>3</sup> Department of Pathology, Haukeland University Hospital, Bergen, Norway, <sup>4</sup> Department of Medicine, Haukeland University Hospital, Bergen, Norway

## INTRODUCTION

- IgA nephropathy (IgAN) is the most prevalent primary chronic glomerular disease worldwide
- Up to 30-50% progress to end stage renal failure
- Recent studies have described the glomerular extracellular matrix (ECM) proteome
- No studies have described ECM changes in glomerular disease

## AIM

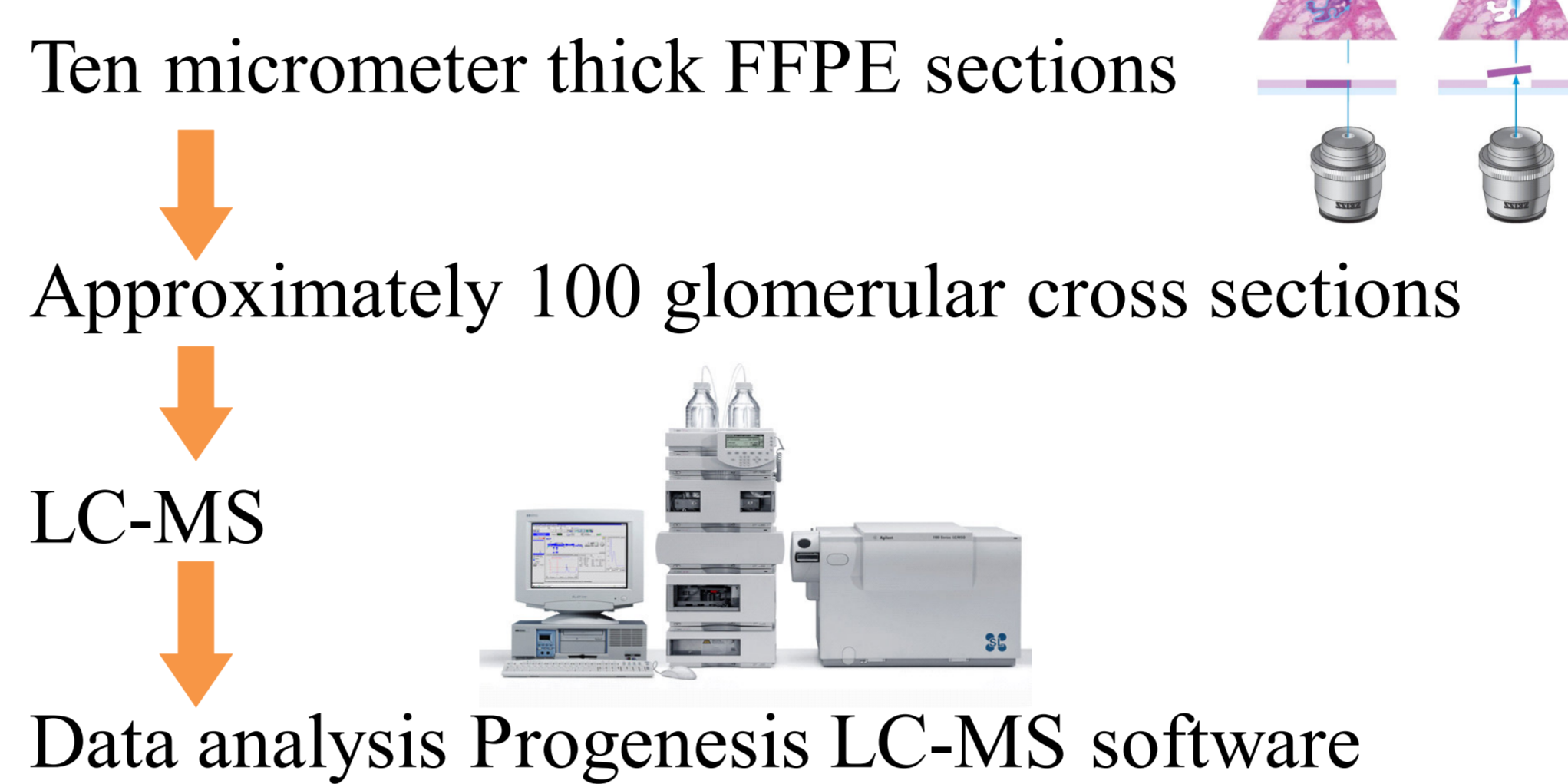
The aim of this study was to characterize the proteomic changes of the glomerular extracellular matrix of patients with IgA nephropathy (IgAN)

## METHODS

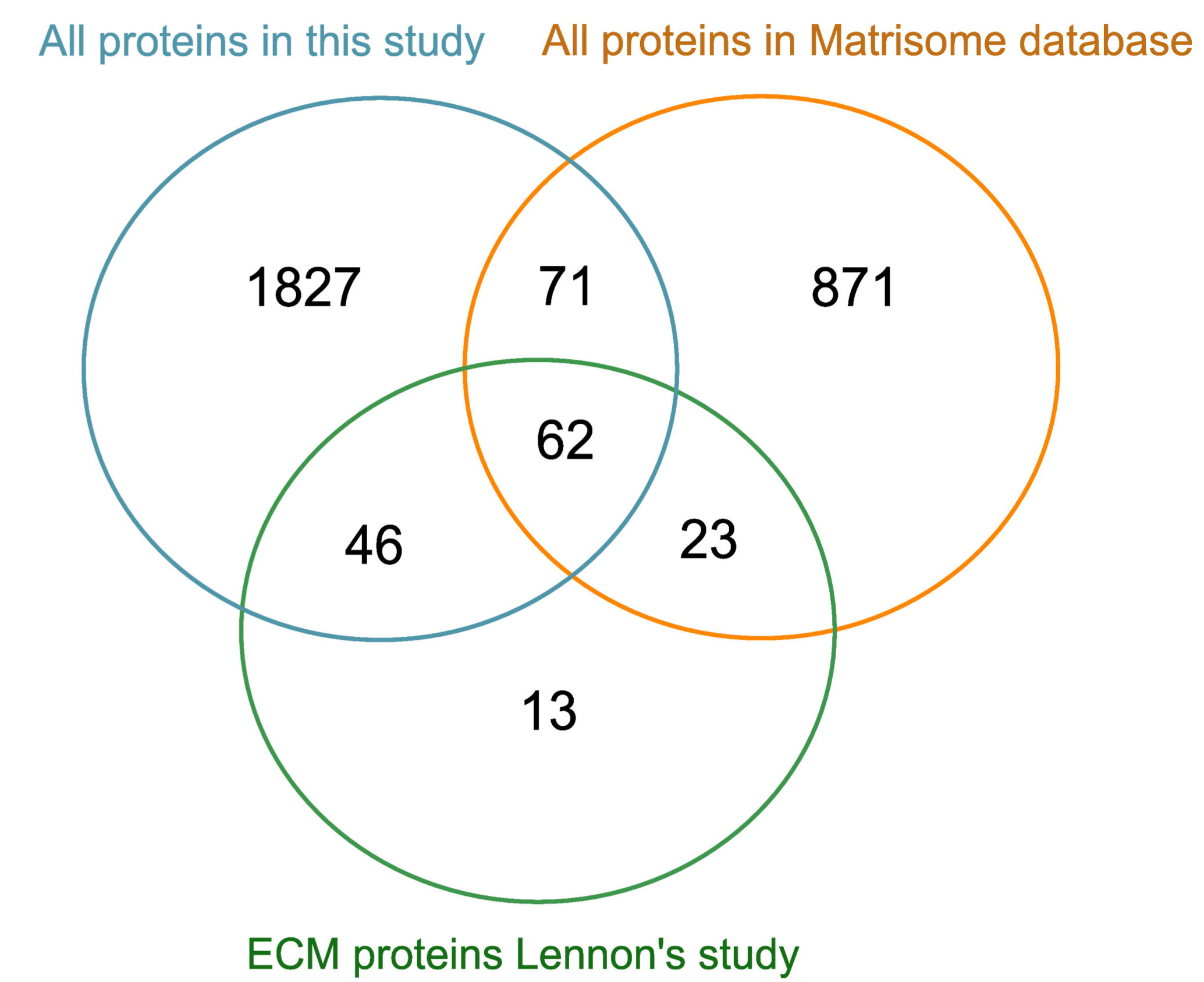
### Study population

25 patients with IgAN  
eGFR >60 ml/min/1.73m<sup>2</sup>  
15 control patients  
eGFR >45 ml/min/1.73m<sup>2</sup>

### Workflow



### Extracellular matrix proteome



## RESULTS

### Patients characteristics

	Controls	IgAN
N	15	25
Year of diagnosis	2000.33 ± 7.7	1996.96 ± 4.4
Proportion female	53.3 %	20 %
Age (years)	32.0 ± 11.9	31.32 ± 13.97
Serum creatinine (mmol/l)	79.3 ± 20.9	96.64 ± 23.6 *
Estimated GFR (ml/min/1.73m <sup>2</sup> )	96.3 ± 24.7	85.92 ± 24.09
Systolic blood pressure (mmHg)	118.6 ± 14.6	130.16 ± 19.18
Diastolic blood pressure (mmHg)	77.6 ± 8.4	78.84 ± 11.90
Urinary protein (grams/24h)	0.15 ± 0.17	1.68 ± 1.03 *
Body weight (kg)	74.7 ± 11.9	75.83 ± 9.85
Percentage with M-score of 1	Not applicable	36 %
Percentage with E-score of 1	Not applicable	32 %
Percentage with S-score of 1	Not applicable	60 %
Percentage with T-score of 1 or 2	Not applicable	16 %

### ECM ASSOCIATED PROTEINS

Protein Name	Gene Name	IgAN vs Control	Fold change	P-value
Azurocidin	AZU1		3,31	0,005
Secreted phosphoprotein 24	SPP2		2,84	0,02
Myeloperoxidase	MPO		2,42	0,0003
Neutrophil elastase	ELANE		2,27	0,006
Matrix metalloproteinase-9	MMP9		2,05	0,0002
Neutrophil defensin 1	DEFA1		1,94	0,0003
Protein S100-A8	S100A8		1,93	0,04
Clusterin	CLU		1,92	0,0001
Protein S100-A4	S100A4		1,87	0,04
Annexin A2	ANXA2		-1,14	0,04
Phosphatidylethanolamine-binding protein 1	PEBP1		-1,30	0,003
Serpin B9	SERPINB9		-1,31	0,02
Carbonic anhydrase 2	CA2		-1,38	0,001
Galectin-3-binding protein	LGALS3BP		-1,46	0,01
Hornerin	HRNR		-1,68	0,04
Syndecan-4	SDC4		-1,79	0,002
Inter-alpha-trypsin inhibitor heavy chain H5	ITIH5		-1,96	0,0002

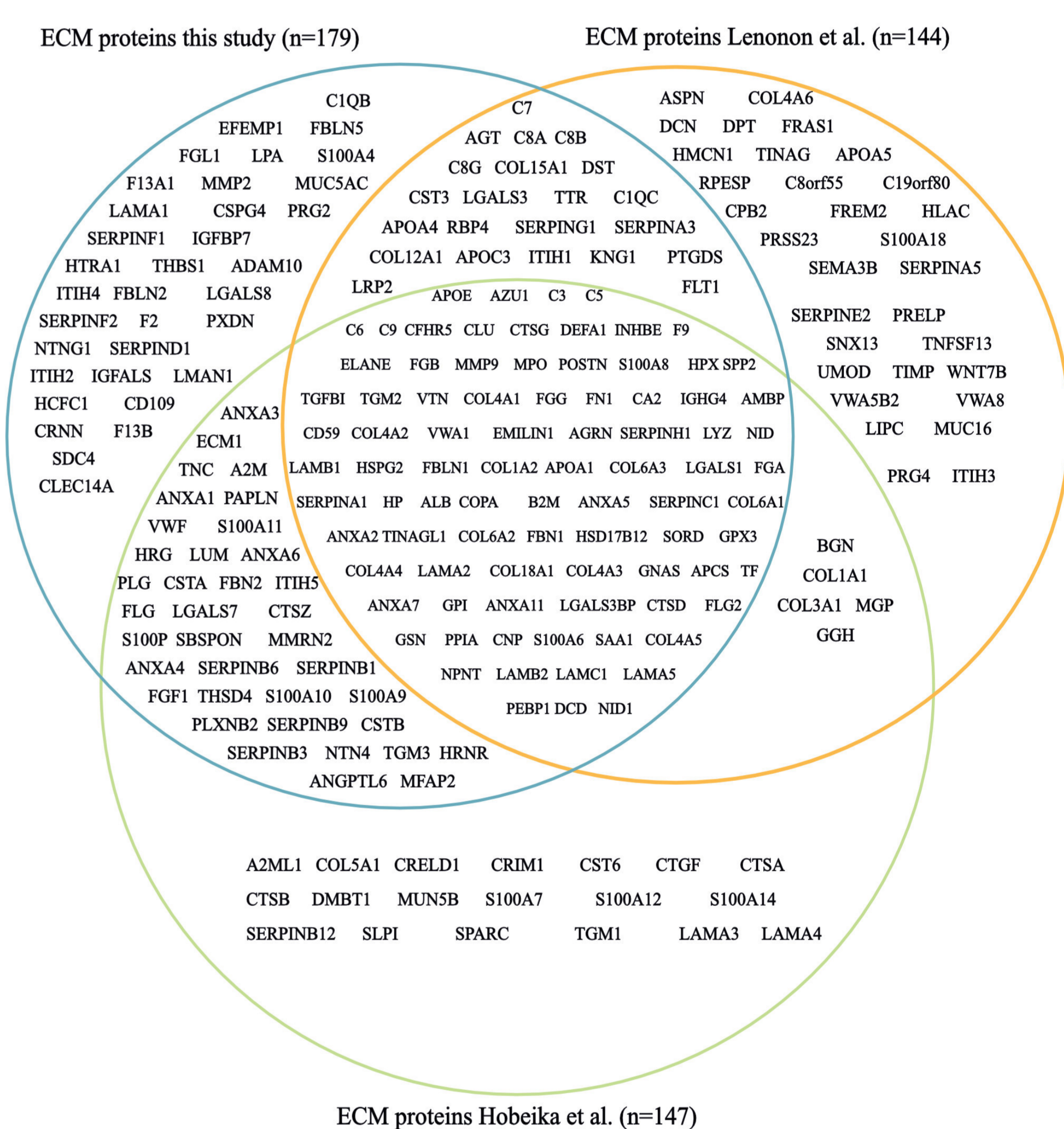
### GLOMERULAR BASAL MEMBRANE PROTEINS

Protein Name	Gene Name	IgAN vs Control	Fold change	P-value
Collagen alpha-1(XV) chain	COL15A1		2,39	0,03
Tenascin	TNC		1,85	0,0001
Collagen alpha-1(IV) chain	COL4A1		1,54	0,000003
Fibronectin	FN1		1,50	0,00004
Collagen alpha-2(IV) chain	COL5A2		1,38	0,0003
von Willebrand factor A domain-containing protein 1	VWA1		1,36	0,01
Nidogen-2	NID2		1,33	0,0004
Laminin subunit beta-1	LAMB1		1,33	0,002

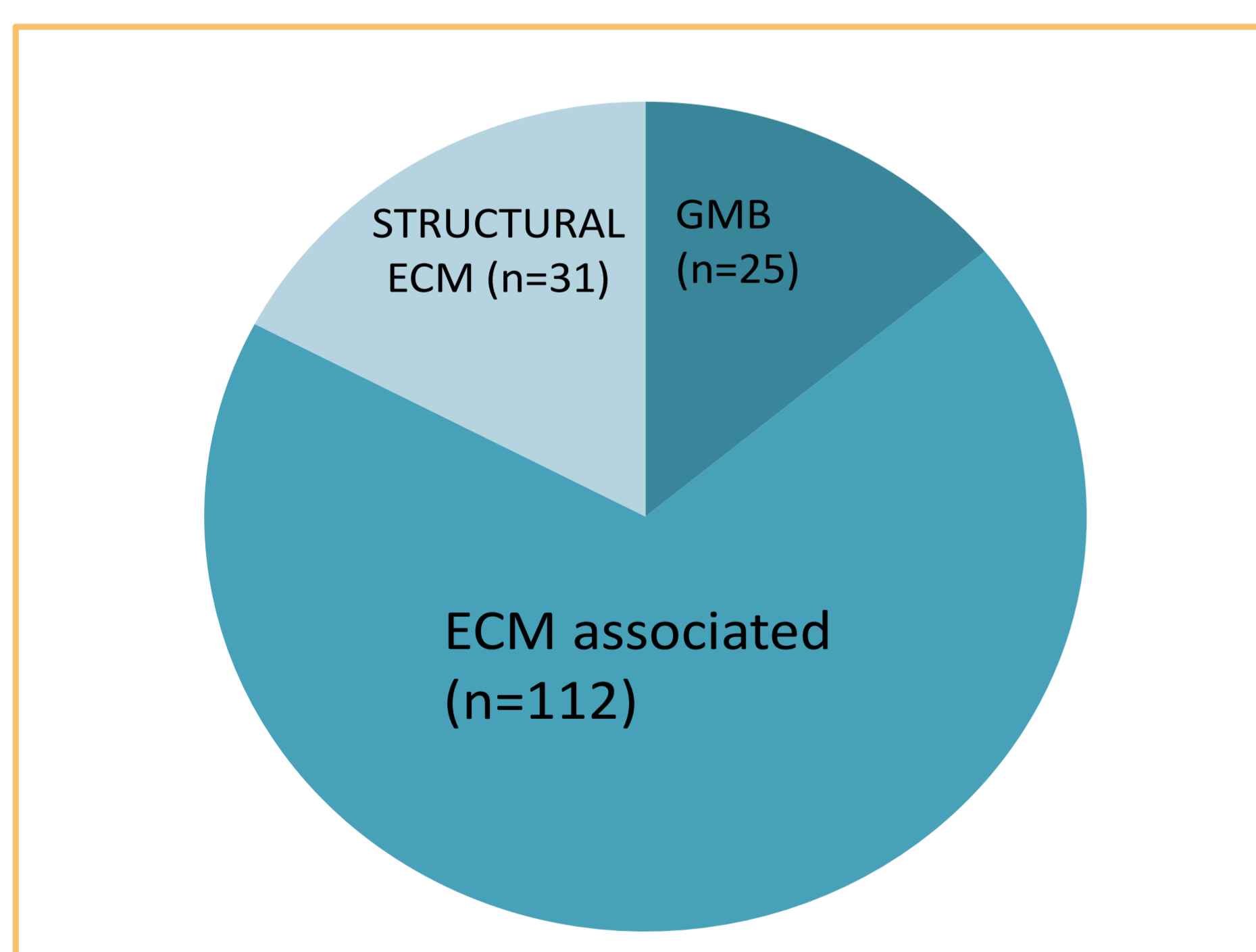
### STRUCTURAL ECM PROTEINS

Protein Name	Gene Name	IgAN vs Control	Fold change	P-value
Periostin	POSTN		3,28	0,000001
EGF-containing fibulin-like extracellular matrix protein 1	EFEMP1		1,89	0,002
Fibrinogen beta chain	FGB		1,87	0,001
Vitronectin	VTN		1,87	0,00001
Transforming growth factor-beta-induced protein ig-h3	TGFBI		1,80	0,001
Extracellular matrix protein 1	ECM1		1,78	0,0003
Fibulin-5	FBLN5		1,76	0,002
Fibrinogen-like protein 1	FGL1		1,60	0,04

### COMPARISON OF OUR DATASET WITH PREVIOUSLY PUBLISHED ARTICLES



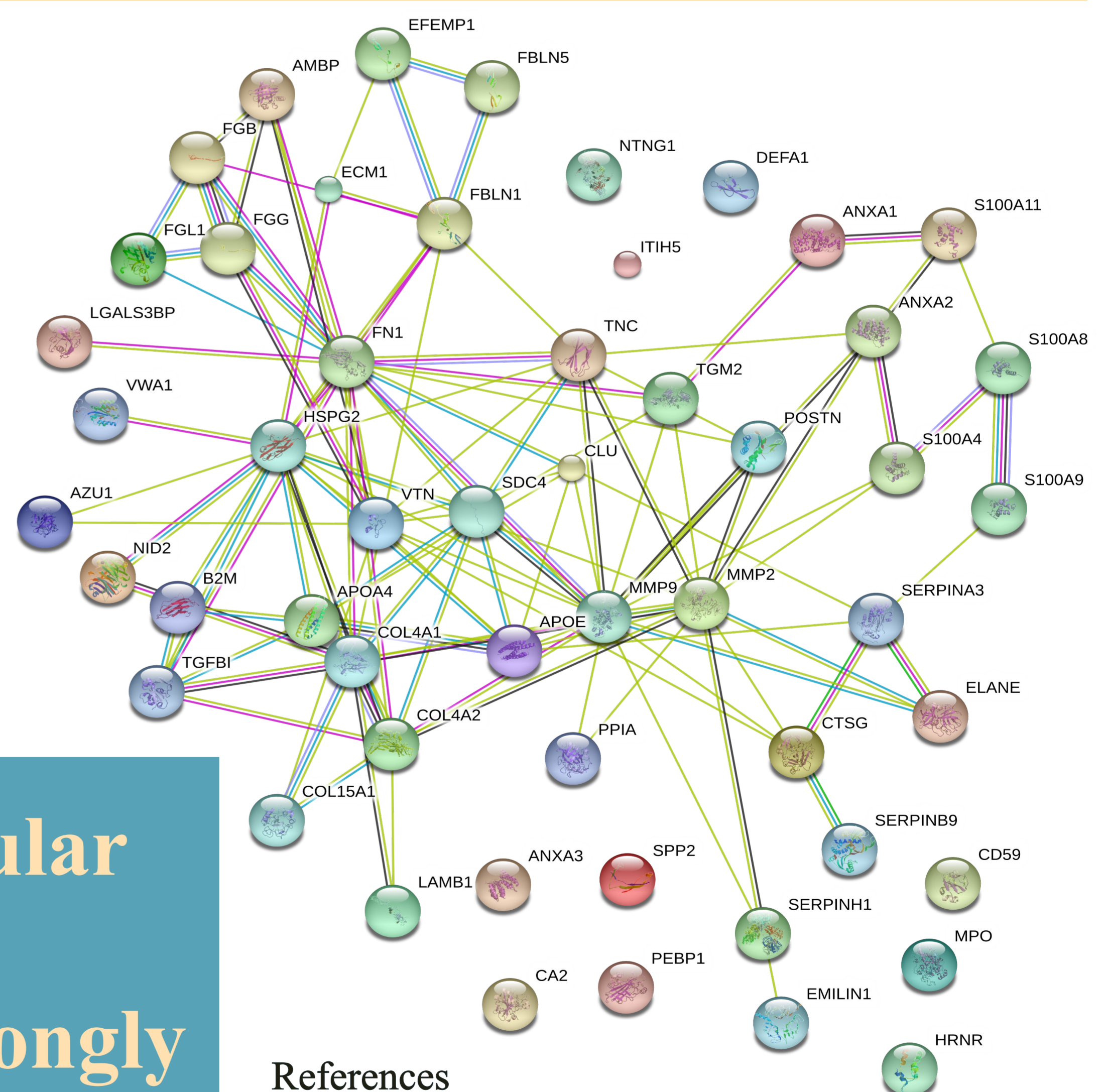
### Classification of ECM proteins



## CONCLUSION

- IgAN is associated with widespread changes of the glomerular extracellular matrix proteome
- Proteins important in fibrosis or inflammation are most strongly increased
- Periostin might be an important marker of glomerular damage in IgA nephropathy

### GLOMERULAR ECM PROTEIN INTERACTION NETWORK



### References

Lennon R, Byron A, Humphries ID, Randles M, Carisley A, Murphy S, et al. Global analysis reveals the complexity of the human glomerular extracellular matrix. *Journal of the American Society of Nephrology*. : JASN. 2014;25(5):939-51.  
Hobeika L, Barati MT, Caster DJ, McLeish KR, Merchant ML. Characterization of glomerular extracellular matrix by proteomic analysis of laser captured microdissected glomeruli. *Kidney International*. 2016.

Contact: flavia\_paunas@yahoo.com

HELSE FONNA

