Increase in serum galactose-deficient IgA1 level measured by new lectin-ELISA predicts progression to kidney failure in adults with IgA nephropathy

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INTRODUCTION

IgA nephropathy (IgAN) is the most common primary glomerular kidney disease in many countries and a leading cause of kidney failure. Its autoimmune pathogenesis begins with elevated circulating galactose-deficient IgA1 (Gd-IgA1) — the initiating autoantigen — which is recognized by IgG autoantibodies, forming immune complexes that deposit in the glomeruli and induce kidney injury.

Prior lectin-based ELISAs were limited by batch-to-batch variability and inconsistent reagent specificity, preventing cross-study comparison. The **GalD™ Assay** addresses this with standardized reagents and calibrated reference standards for reproducible measurement.

AIM

To assess whether percent change in serum Gd-IgA1, measured by the standardized **GalD™ Assay**, independently predicts progression to kidney failure in adults with biopsy-confirmed IgAN.

METHOD

- Serum Gd-IgA1 was measured using the **GalD™ Assay** in paired samples from **245 adults** with biopsy-confirmed IgAN in CureGN, an NIH-funded multicenter longitudinal observational cohort.
- Paired samples were collected at ~1-year intervals (median: **13.3 months**); median follow-up was **8.5 years**.
- Kidney failure was defined as chronic dialysis, transplantation, or two consecutive eGFRs <15 mL/min/1.73 m² ≥30 days apart (20% event rate).
- Cox proportional hazards modeling assessed percent change in Gd-IgA1 as an independent predictor, adjusted for age, eGFR, UPCR, race, RAAS inhibitor use, and immunosuppressant use.

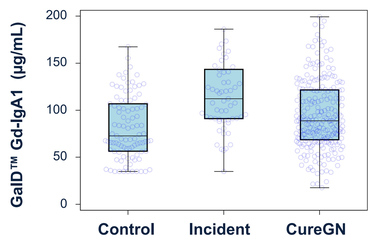
RESULTS

Baseline Patient Characteristics

Characteristic	Total (N = 245)
Demographics	
Age at first sample, years, Median (IQR)	42 (31, 55)
Male sex, n (%)	135 (55%)
Race, n (%)	
White / Caucasian	186 (76%)
Asian	35 (14%)
Black / African American	8 (3%)
Other / Unknown	16 (7%)
Hispanic ethnicity, n (%)	41 (17%)
Disease Characteristics at First Sample	
eGFR, mL/min/1.73 m², Median (IQR)	58 (42, 86)
UPCR, g/g, Median (IQR)	0.9 (0.2, 1.7)
Hypertension, n (%)	141 (58%)
Hematuria ≥1+, n (%)[1]	121 / 183 (66%)
Treatment at First Sample	
RAAS inhibitor, n (%)	196 (80%)
Immunosuppression, n (%)	72 (29%)
Study Timeline	
Time from biopsy to first sample, months, Median (IQR)	15.8 (5.0, 37.8)
Interval between paired samples, months, Median (IQR)	13.3 (10.7, 15.2)
Follow-up from first sample, years, Median (IQR)	8.5 (6.5, 9.4)
Outcome	
Kidney Failure events, n (%)	49 (20%)

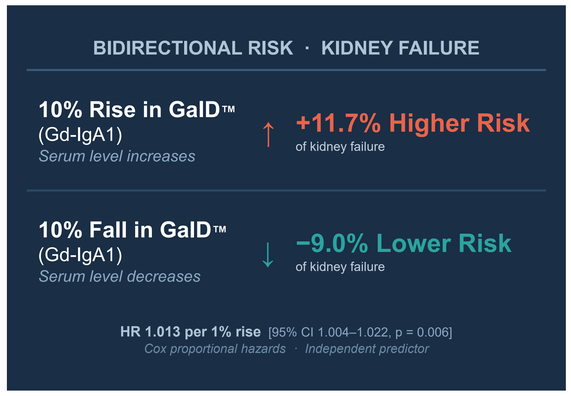
[1] Hematuria data were unavailable for 62 participants (25%); percentage calculated from 183 with evaluable dipstick result. eGFR = estimated glomerular filtration rate; IQR = interquartile range; RAAS = renin-angiotensin-aldosterone system; UPCR = urine protein-to-creatinine ratio; kidney failure = end-stage kidney disease (chronic dialysis, kidney transplantation, or two consecutive eGFRs <15 mL/min/1.73 m² ≥30 days apart).

Distribution Analysis: Control | Incident | CureGN



Box and Whisker plots comparing **GalD™** Gd-IgA1 distribution for the 245 CureGN IgAN patients with prior **GalD™** analysis of 97 healthy controls and 61 biopsy-proven IgAN incident samples.

Distribution Analysis Data: Percentile values for Box and Whisker Plots						
Cohort	**N**	**5%**	**25%**	**50%**	**75%**	**95%**
Control	97	35.00	56.40	72.70	106.90	140.20
Incident	61	59.20	91.10	112.30	143.50	261.20
CureGN	245	41.58	68.59	88.79	121.58	172.89



GalD™ Assay Values and Primary Outcomes

GalD™ Assay — Serum Gd-IgA1 Values (N = 245)	Median (IQR)
Absolute Serum GalD™ Gd-IgA1 (µg/mL)	
First sample	88.8 (68.6, 121.6)
Second sample	90.1 (69.3, 119.0)
Change Between Paired Samples	
Absolute change, µg/mL	1.5 (−11.4, 10.6)
Percent change, %	1.5 (−13.5, 11.6)
Primary Result — Adjusted Cox Model	
Hazard ratio per 1% rise in GalD™ Gd-IgA1 [95% CI]	1.013 [1.004, 1.022]
p-value	0.006
Covariates adjusted	Age, eGFR, UPCR, race, RAAS inhibitor, immunosuppression



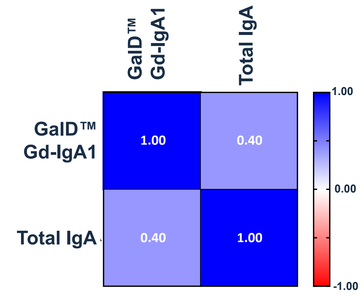
A Lectin-Based Quantification of Serum Galactose-deficient IgA1

- **Quantitative assay**
- **4-hour turn-around**
- **96-well plate**



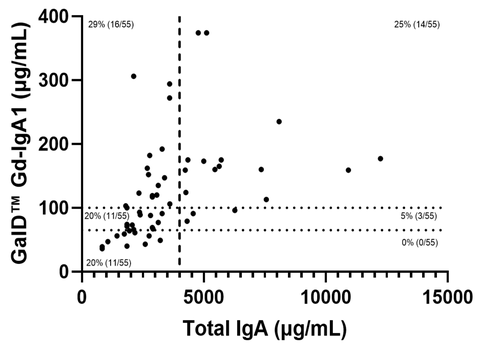
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Gd-IgA1 is Not Explained by Total IgA



Pearson correlation between GalD™ Gd-IgA1 and Total IgA across 55 serum samples. The two were only weakly correlated ($r = 0.40$, $r^2 = 0.16$), indicating that ~84% of the variation in GalD™ Gd-IgA1 is independent of total IgA.

GalD™ Gd-IgA1 vs. Total IgA



GalD™ Gd-IgA1 vs. Total IgA. Scatter plot of serum GalD™ Gd-IgA1 against total serum IgA for 55 biobank samples. Horizontal dotted lines mark GalD™ Gd-IgA1 thresholds set near the control median (≈75 µg/mL, moderate) and 75th percentile (≈100 µg/mL, high); these are rounded to practical values rather than exact percentiles. The vertical dashed line marks the upper limit of the normal total IgA range (4000 µg/mL). Sample counts and percent of cohort are shown for each region. Notably, no sample (0/55) had elevated Total IgA with low GalD™ Gd-IgA1, while most samples with elevated GalD™ Gd-IgA1 had normal Total IgA consistent with GalD™ Gd-IgA1 varying independently of total IgA.

REFERENCES

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CONCLUSIONS

- Percent change in serum Gd-IgA1, measured by the GalD™ Assay, is an independent predictor of kidney failure in adults with IgAN — after full adjustment for eGFR, proteinuria, age, race, and treatment.
- A 10% rise in GalD™ Gd-IgA1 corresponds to +11.7% higher risk of kidney failure; a 10% fall to −9% lower risk — a bidirectional, clinically actionable signal.
- These findings directly support KDIGO 2025 guidelines recommending monitoring of pathogenic IgA1 (Gd-IgA1) as a treatment target in IgAN.

CONTACT INFORMATION

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