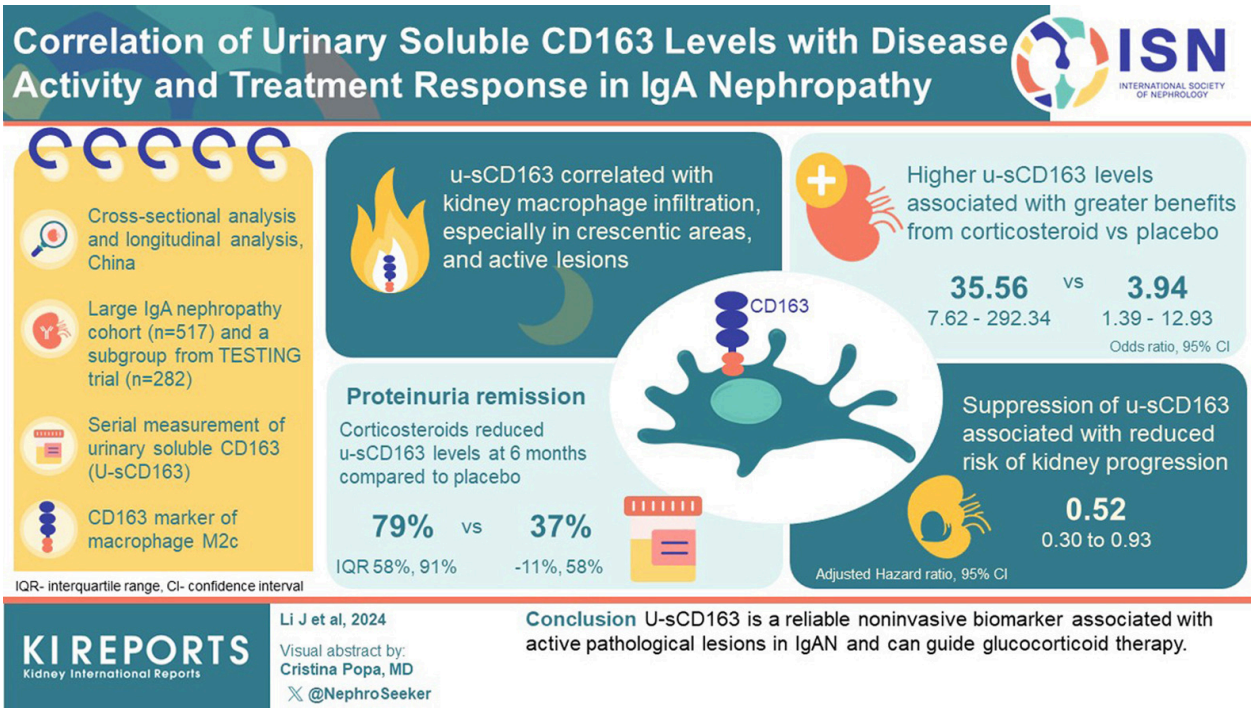
1/ What if there was a biomarker that could guide therapeutic decision-making in patients with IgA Nephropathy (IgAN)? 🤔

Today, we will discuss a study by Li, J., et.al. that explores this potential biomarker ❗

Read the study here ➡️ https://www.kireports.org/article/S2468-0249(24)01861-8/fulltext

Beautiful visual abstract 🤩 by @NephroSeeker



2/ More than half of the patients with IgAN will progress to kidney failure requiring dialysis and/or kidney transplantation. Although supportive care is given for all patients, a careful risk/benefit analysis is needed when considering corticosteroids given their side effect profile

3/ This article's commentary by Li G & Thanabalasingam SJ @thana_susan (https://www.kireports.org/article/S2468-0249(24)01883-7/fulltext) cite a recent study by Harada, K., et.al. that showed glucocorticoid responders had ⬇️ # of fibroblast-specific protein 1-positive (FSP1+) in the renal tissue vs. non responders.

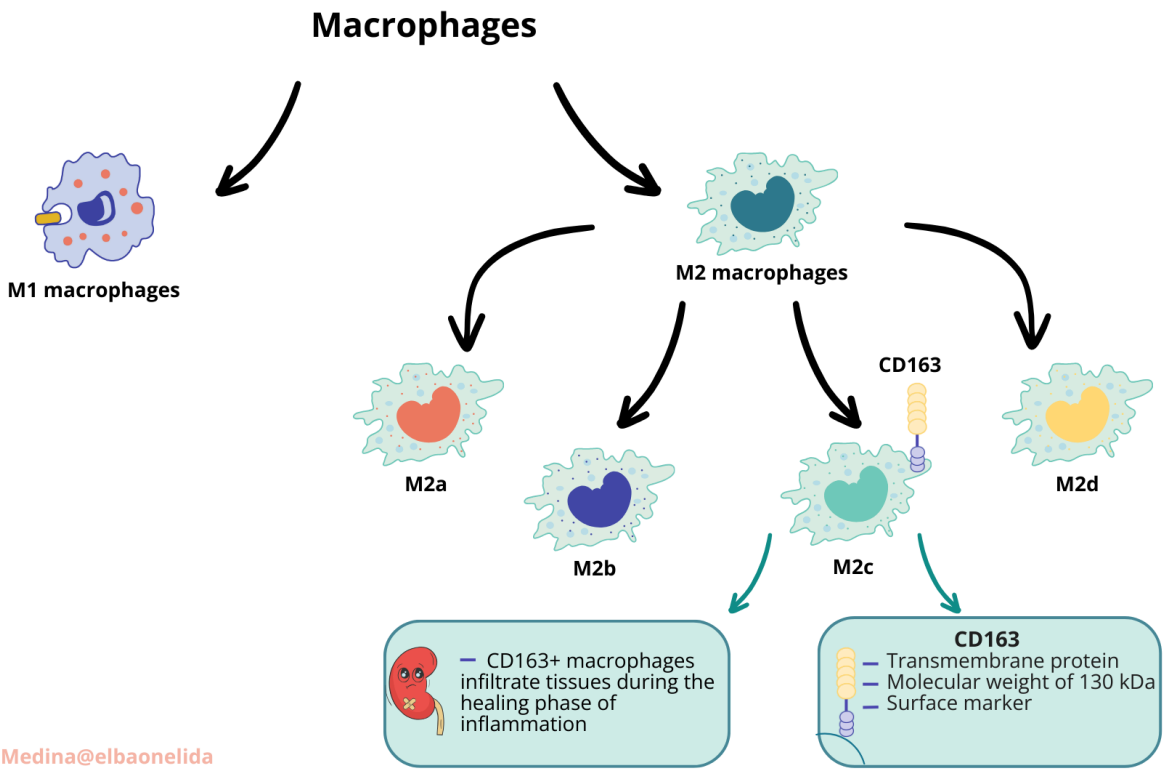
4/ Also, the # of FSP1+ cells predicted corticosteroid responsiveness, since patients who had >32.6 FSP1+ cells/HPF at dx were more likely to exhibit steroid resistance.

5/ The downside of FSP1+ cells is the need to be detected from renal tissue which requires an invasive procedure and will also limit their use and utility for monitoring purposes.

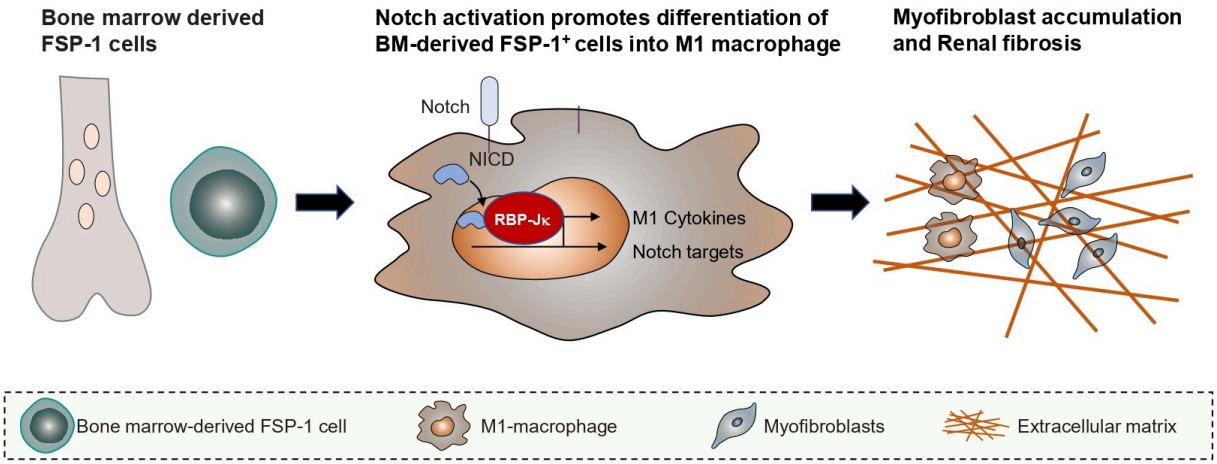
6/ [Poll] Shifting gears…
which of these cells play an important role in the progression of IgAN?

- Plasma cells
- Macrophages
- T cells

7/ Increasing evidence suggests that the mononuclear or macrophage system plays an important role in the progression of IgAN. Macrophages can be broadly categorized into classically activated macrophages and M2 macrophages.



7 8/ In mice with obstructed kidneys, most FSP-1+ cells are activated macrophages ➡️from bone marrow. Notch signaling activates the production of M1 cytokines in FSP-1+ monocytes/macrophages➡️ important for renal inflammation and fibrosis.
https://pubmed.ncbi.nlm.nih.gov/36672147/



9/ CD163 is a transmembrane protein expressed as a surface marker by M2c macrophages. In IgAN CD163+ macrophages in glomeruli were associated with ⬇️ eGFR and the presence of crescents. However, what about urinary soluble CD163 (u-sCD163)?

10/ In the cross-section study of 517 patients, levels of u-sCD163 at baseline were strongly correlated with:
⬇️ eGFR & serum albumin
⬆️ proteinuria & microscopic hematuria

Table 1. Clinicopathological features of IgAN cohort patients

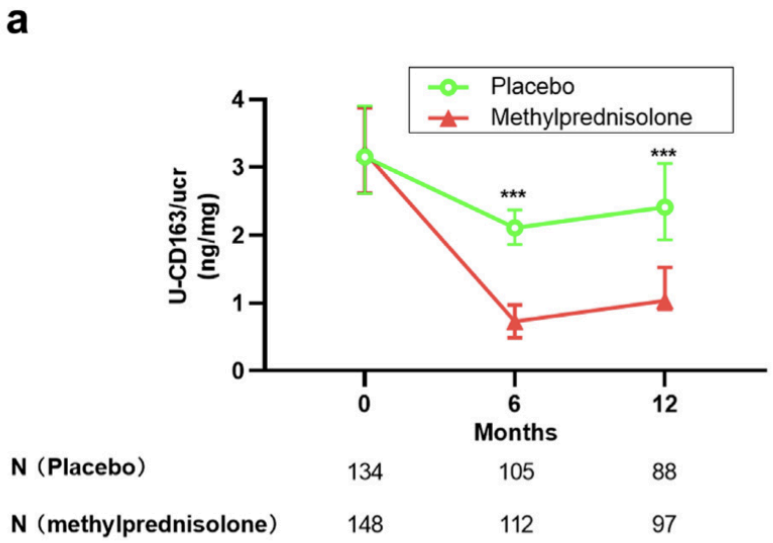
	1 n = 129	2 n = 130	3 n = 129	4 n = 129	P^a	P^b
Sex, male (n, %)	92 (71%)	73 (56%)	65 (50%)	45 (35%)	<0.001	<0.001
Age (yr)	35 ± 10	37 ± 12	38 ± 13	41 ± 16	0.024	<0.001
MAP (mm Hg)	97 ± 11	95 ± 11	95 ± 10	97 ± 13	0.258	0.877
Systolic BP (mm Hg)	128 ± 14	126 ± 16	127 ± 14	130 ± 18	0.232	0.435
Diastolic BP (mm Hg)	82 ± 10	80 ± 11	80 ± 10	81 ± 12	0.330	0.705
Proteinuria (g/24 h)	1.65 (1.28–2.32)	1.86 (1.41–2.77)	2.44 (1.62–4.10)	3.77 (2.43–5.9)	<0.001	<0.001
Scr (μmol/l)	115 (82.6–156)	107.8 (79.5–145)	108 (77.6–183.2)	113.2 (74.6–168.1)	0.889	0.212
eGFR (ml/min per 1.73 m^2)	71 (47–95)	74 (44–94)	66 (36–99)	55 (37–90)	0.154	0.058
Hematuria (RBCs/ul)	22.0 (8.3–61.8)	35 (12.5–157)	65.3 (17.5–190)	101.1 (36.9–503.8)	<0.001	<0.001
Albumin (g/l)	40.1 ± 4.4	37.7 ± 4.8	34.6 ± 6.6	31 ± 6.5	<0.001	<0.001
Oxford's classification (n, %)						
M1	69 (53%)	76 (58%)	84 (65%)	80 (62%)	0.26	0.095
E1	35 (27%)	41 (32%)	51 (40%)	90 (70%)	<0.001	<0.001
S1	92 (71%)	99 (76%)	87 (67%)	79 (61%)	0.065	0.032
T1/T2	45 (35%)/13 (10%)	52 (38%)/11 (9%)	50 (39%)/23 (18%)	52 (40%)/19 (15%)	0.088	0.025
C1/C2	64 (50%)/10 (8%)	71 (55%)/20 (15%)	65 (50%)/24 (19%)	69 (53%)/40 (31%)	<0.001	<0.001

BP, blood pressure; C, crescents; eGFR, estimated glomerular filtration rate; E, endocapillary hypercellularity; IgAN, IgA nephropathy; M, mesangial hypercellularity; MAP, mean arterial pressure; RBCs, red blood cells; Scr, creatinine; S, segmental glomerulosclerosis; T, interstitial fibrosis and tubular atrophy.
[a]Among the 3 groups.
[b]P for trend.
Unless otherwise indicated, the values represent n (%), the mean ± SD, or the median (25th–75th centiles).

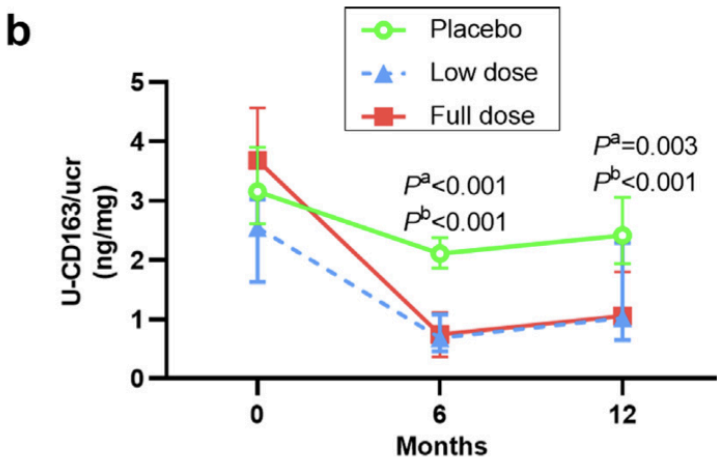
11/ ⬆️ u-sCD163 levels correlated with ⬆️ of E and C lesions scores (from MEST-C score)

12/ ⬆️ of u-sCD163 had ⬆️ odds ratio to reach proteinuria remission at 6 months and more likely to benefit from corticosteroid therapy

13/ Methylprednisolone ⬇️ levels of u-sCD163 at 6 months [79% vs. 37%] and at 12 months [65% vs 34%] compared to placebo



14/ There was no difference of u-sCD163 levels between full dose and reduced dose of corticosteroid regimen.



N（Placebo）	133	105	88
N（low dose）	44	34	33
N (full dose)	104	78	64

15/ ⬇️ of u-sCD163 had lower risk of kidney progression events 🫘📉

16/ Questions that remain unanswered:
Will budesonide lead to changes in u-sCD163?
Does ⬆️ u-sCD163 levels in glucocorticoids responders imply a relapse of IgAN?
Will a significant ⬇️ of u-sCD163 accompany a remission of proteinuria from supportive therapy alone?

17/ Other important limitation was external validity since this paper was limited to a Chinese population 🇨🇳 since not all sites from the testing study did the biobanking subgroup 👩‍🎨

18/ u-sCD163 proves to be a potential and convenient (no need of kidney biopsy) biomarker that predicts a patient's prognosis and/or response to glucocorticoids in IgAN.

19/ Let's have another final poll. How much have you learned today ? Levels of u-sCD163 at baseline were strongly correlated with?
Decrease of eGFR & serum albumin
Decrease proteinuria
Decrease microscopic hematuria