小球厚基底膜肾病

GCBM ⟶ **TGCBM**

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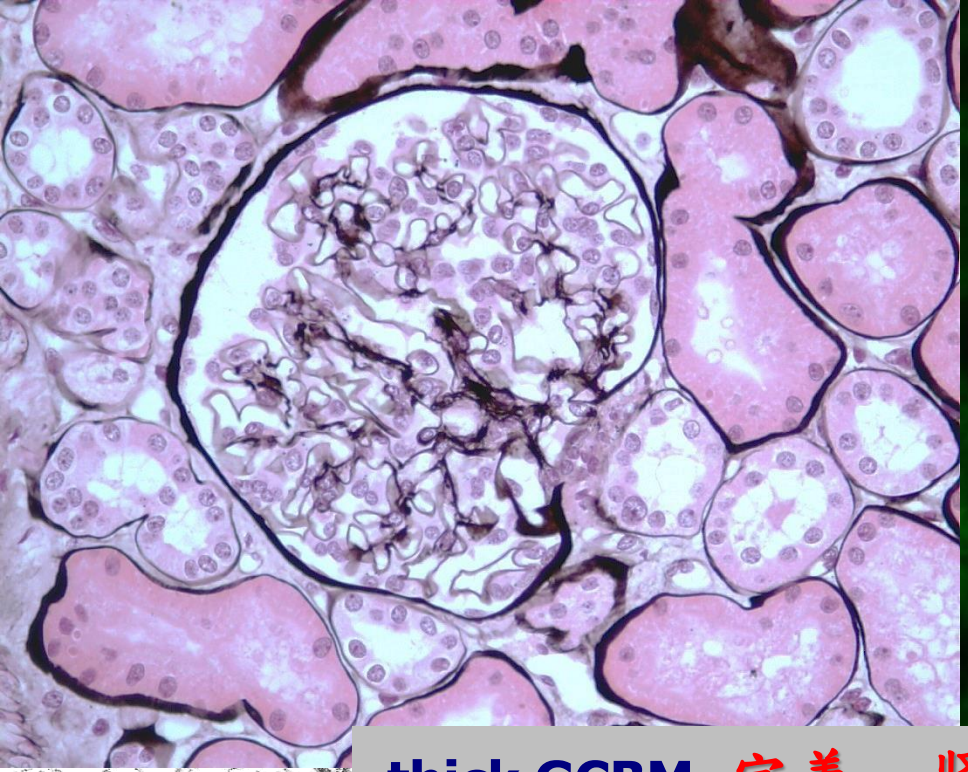
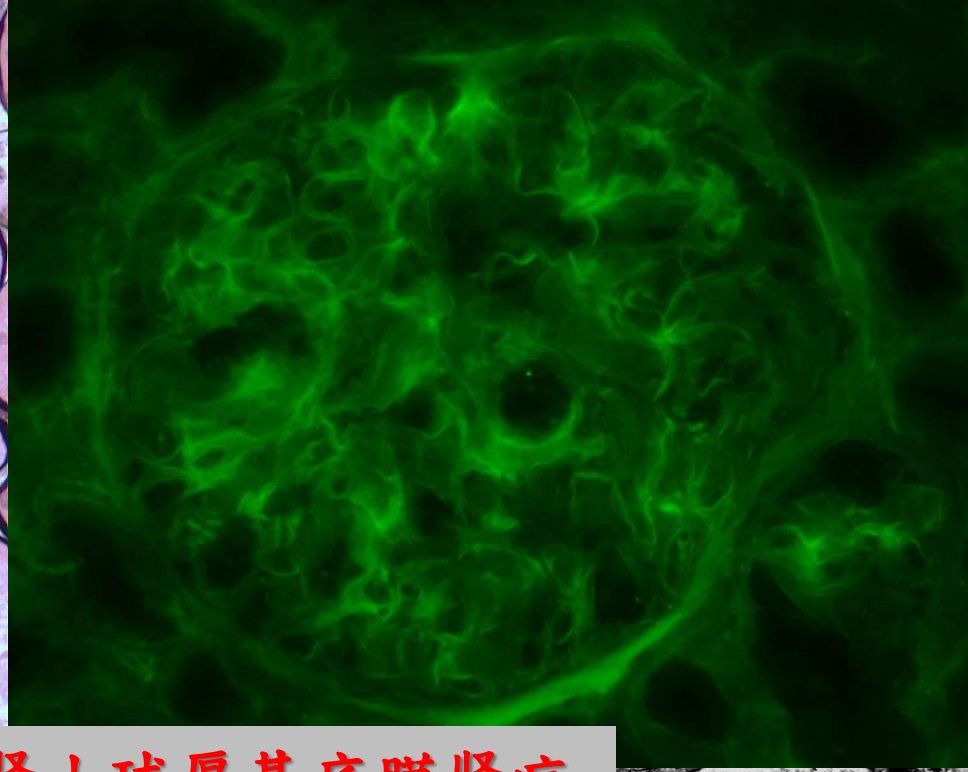
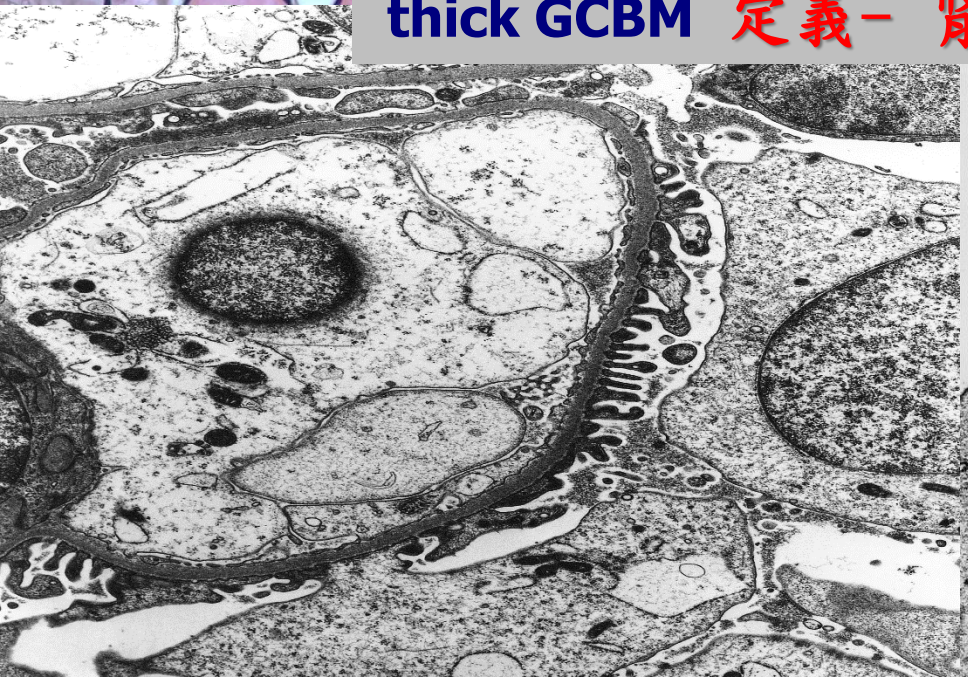
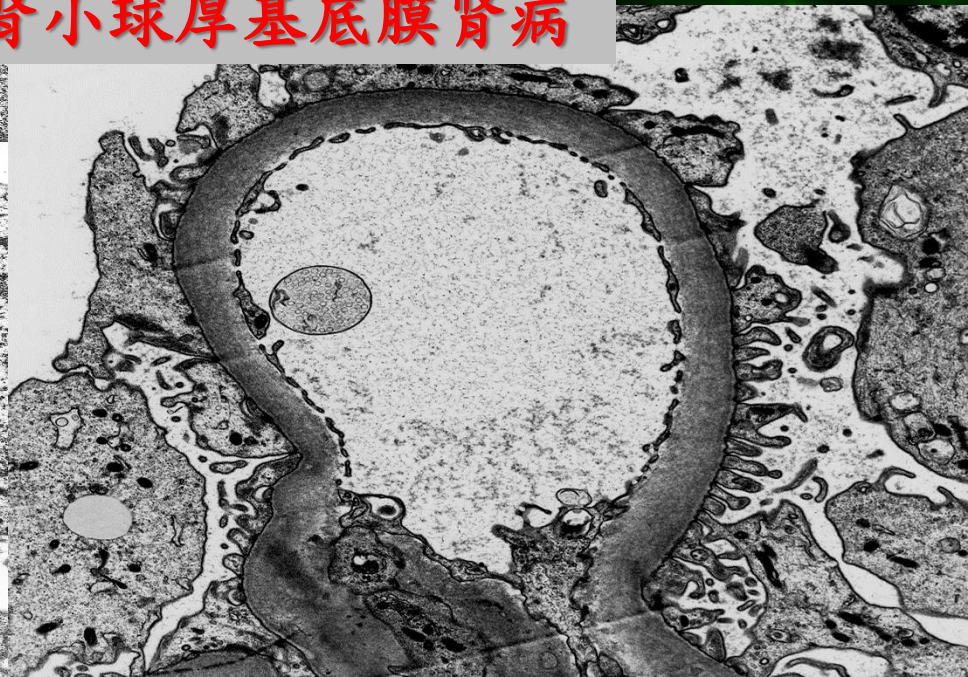
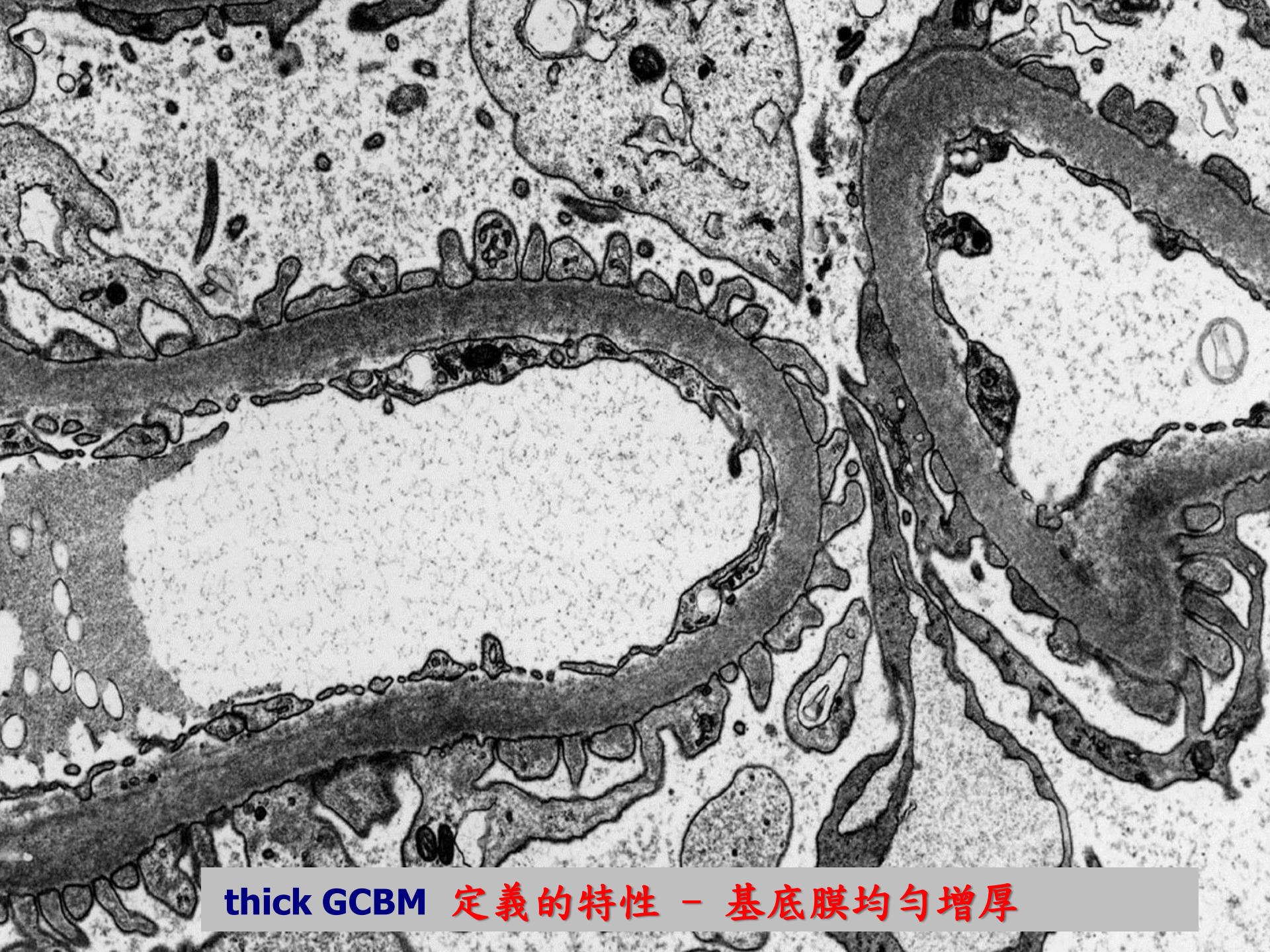




thick GCBM 定義– 腎小球厚基底膜腎病







thick GCBM 定義的特性 – 基底膜均勻增厚

thick GCBM 定量測量 – 基底膜厚度 > 400 nm (346 – 396 nm)

TGCBM – Clinical Presentation 腎病臨床表現

groups 分组	age (range) 年龄	proteinuria (nephrotic) 蛋白尿 (>3.5 g)	proteinuria g/24 hr 24 h尿蛋白定量	HM 血尿	HTN 高血壓	diabetic retinopathy 視網膜病變	Scr µmol/l 血肌酐
controls 對照 (13)	46 (22-60)	61% (0)	0.80	8%	0	0/10	63
TGCBM (12M:11F)	**48 (22-74)**	**87% (26%)**	**2.95**	**35%**	**48%**	**0/13**	**102**
早期糖尿病 early DM (11)	47 (26-64)	91% (46%)	5.24	36%	46%	1/10	85
晚期糖尿病 late DM (34)	47 (20-79)	100% (44%)	4.14	41%	47%	18/26	234

isolated diffuse TGCBM: a renal lesion in prediabetes? Lai FM et al, Mod Pathol 2004;17:1506

TGCBM – pre-diabetes? 與糖尿病的關係?

Fasting B Glucose 空腹血糖	at time of biopsy 腎活檢時	6 months follow-up 隨訪6個月時	48 months follow-up 隨訪48個月時
patients tested 測試患者	10	18	23
normal FPG < 5.5 mmol/l 空腹血糖正常	8 (80%)	10 (56%)	6 (26%)
IFG 5.5-6.9 mmol/l 空腹血糖異常	-	2 (11%)	5 (22%)
IGT 糖耐量異常	-	2 (11%)	4 (17%)
diabetes ≥ 7 mmol/l 糖尿病	2 (20%)	4 (22%)	8 (35%)

isolated diffuse TGCBM: a renal lesion in prediabetes? Lai FM et al, Mod Pathol 2004;17:1506

TGCBM – Pathogenesis 厚基底膜發病機制

hyperglycemia
高血糖
microangiopathy: glomerulosclerosis, hyaline a.

insulin resistance (HOMA, insulinemia)
胰島素抵抗和高胰島素血症
macroangiopathy: atherosclerosis

hemodynamic and hyperfiltration
血流動力學改变和高濾过
glomerulosclerosis

Genetic: THBS1,COX1, COX2, MMP9, GLUT1?
遺傳因素

Glomerular hypertrophy is associated with hyperinsulinemia and precedes overt diabetes in aging rhesus monkeys.
Cusumano AM et al. Am J Kidney Dis 40:1075, 2002

小球肥大（厚基底膜）与糖尿病之前的高胰島素血症相关

TGCBM – 24例厚基底膜患者的胰島素抵抗表現

GCBM thickness	基底膜厚度	468 nm	408 - 659
proteinuria at biopsy	蛋白尿量	1.82 g/day	0.4 – 3.9
creatinine at biopsy	血肌酐水平	110 umol/l	52 – 230
impaired renal function (>130)	腎功能異常	5	21%
follow-up period	隨訪时间	45 months	5 – 88
Serum Insulin (fasting)	血清胰島素水平	64.74 pmol/l	6.8 – 144.6
hyperinsulinemia >60 pmol/l	高胰島素血症	19	62.5%
HOMA (Homeostasis Assessment Model)	穩態模型評估	2.13	0.31 – 5.07
Insulin Resistance (+HOMA) (M >2.42, F >2.08)	胰島素抵抗度	13	54.2%
diabetic	糖尿病	3/19	16%
abnormal GTT	糖耐量異常	5/19	26%

“Journey to the West” : Fact or Fiction?..TGCBM. Lai FM et al, HK J Nephrol 2008;10:50-57

GCBM thickness in selected biopsies

Insulin Resistant States 臨床胰島素抵抗狀態

2009 data	例數 number of cases	薄基底膜 < 300 nm	正常厚度 GCBM 346-396 nm	厚基底膜 > 400 nm	6個月內糖尿病的发病率
diabetics 糖尿病	80	0	12	68	100%
TGCBM 厚基底膜	98	-	-	98	43% （35/81)
IgAN IgA 腎病	126	14	63	44	29% (11/38)
MCN 微小病變腎病	118	9	63	37	33% (7/21)
Allograft 腎移植	53	0	11	39	47% (16/34)
Thin MN薄基底膜腎病	113	113	1	2	2

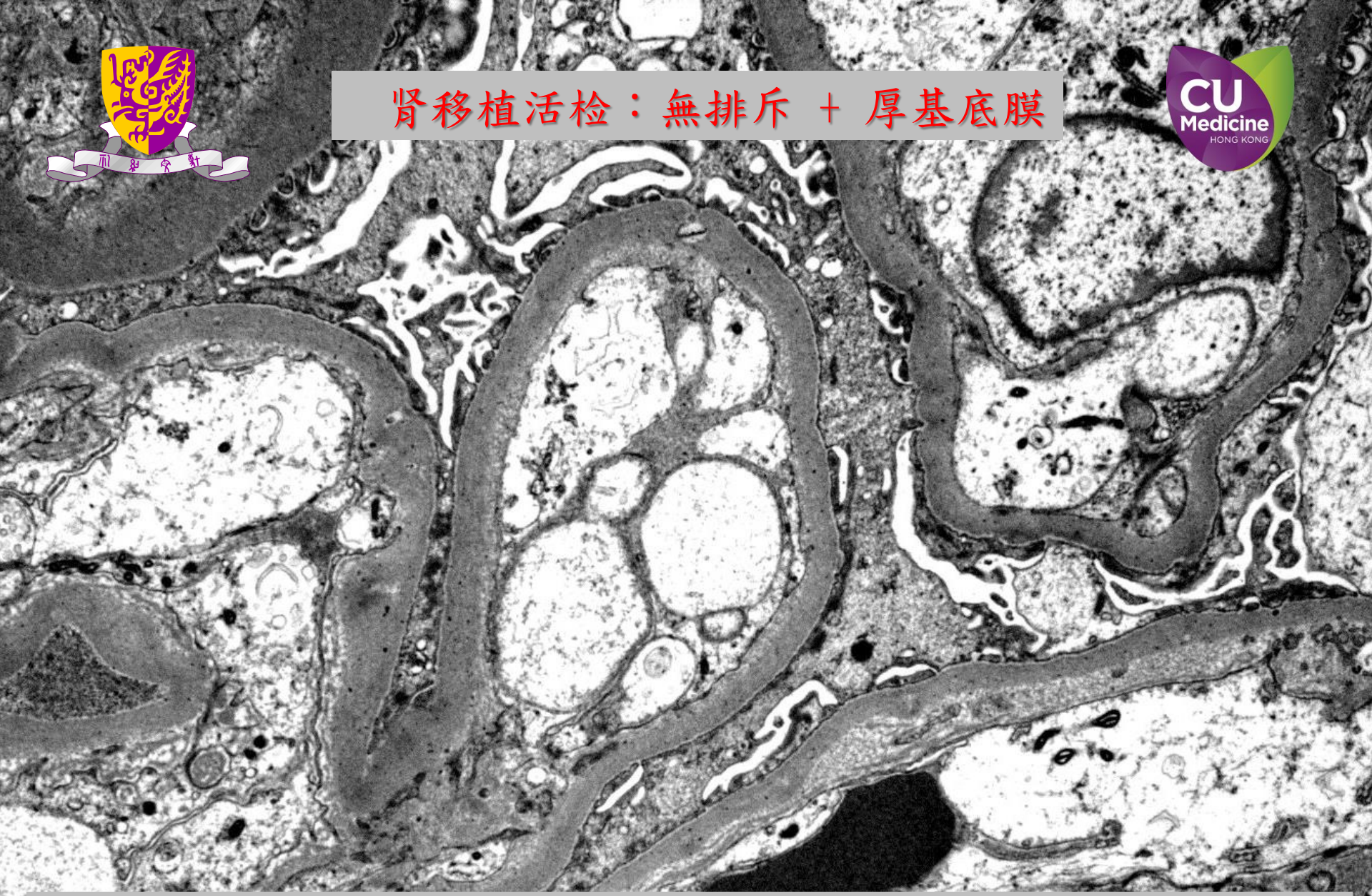
3 separate groups of patients :

1. early-diabetes
2. on steroids therapy
3. not diabetic, nor on steroids

可識別三类獨立的患者群體:

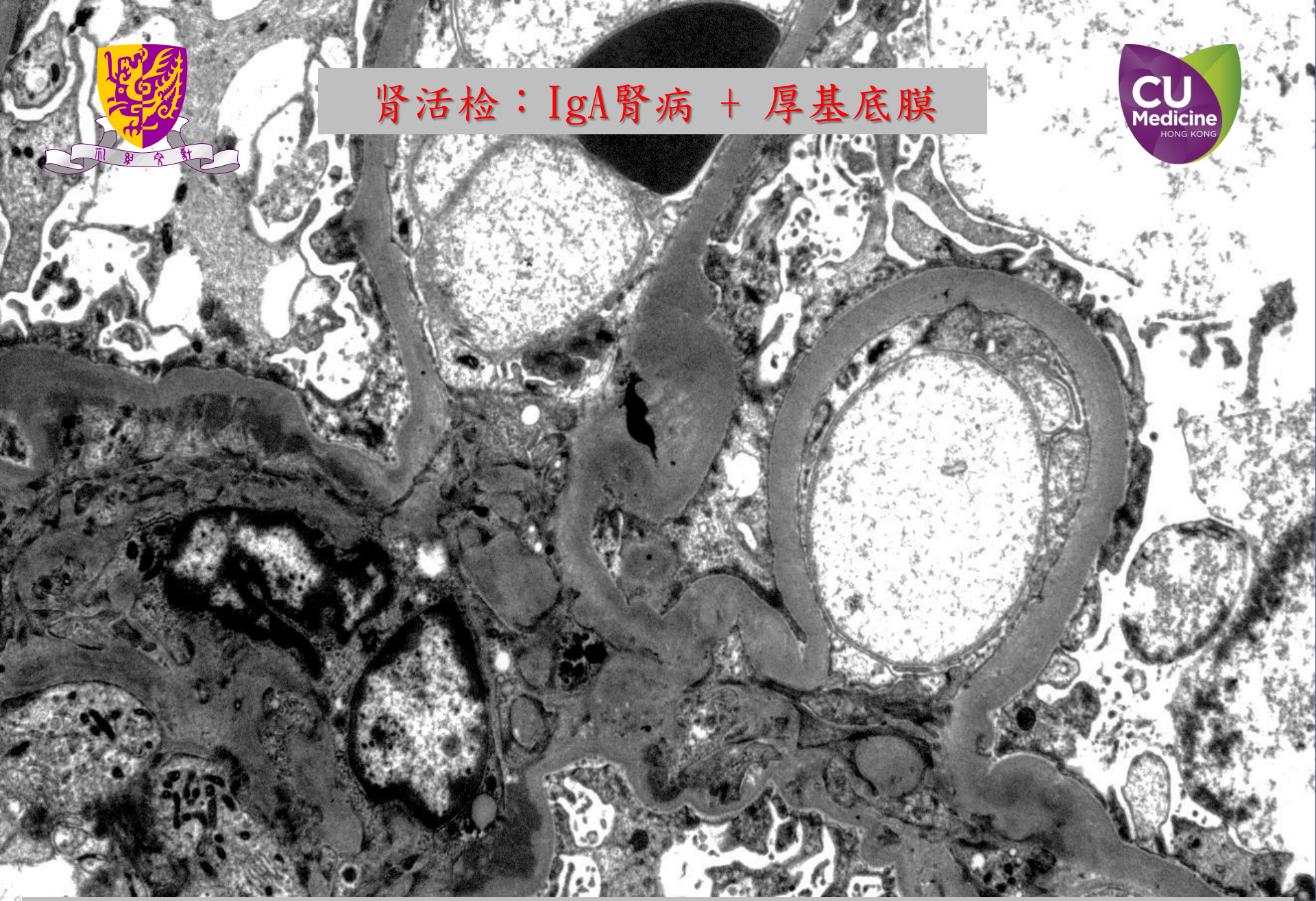
1. 早期糖尿病
2. 服類固醇的患者
3. 沒有糖尿病，也沒有服類固醇

肾移植活检：無排斥 + 厚基底膜



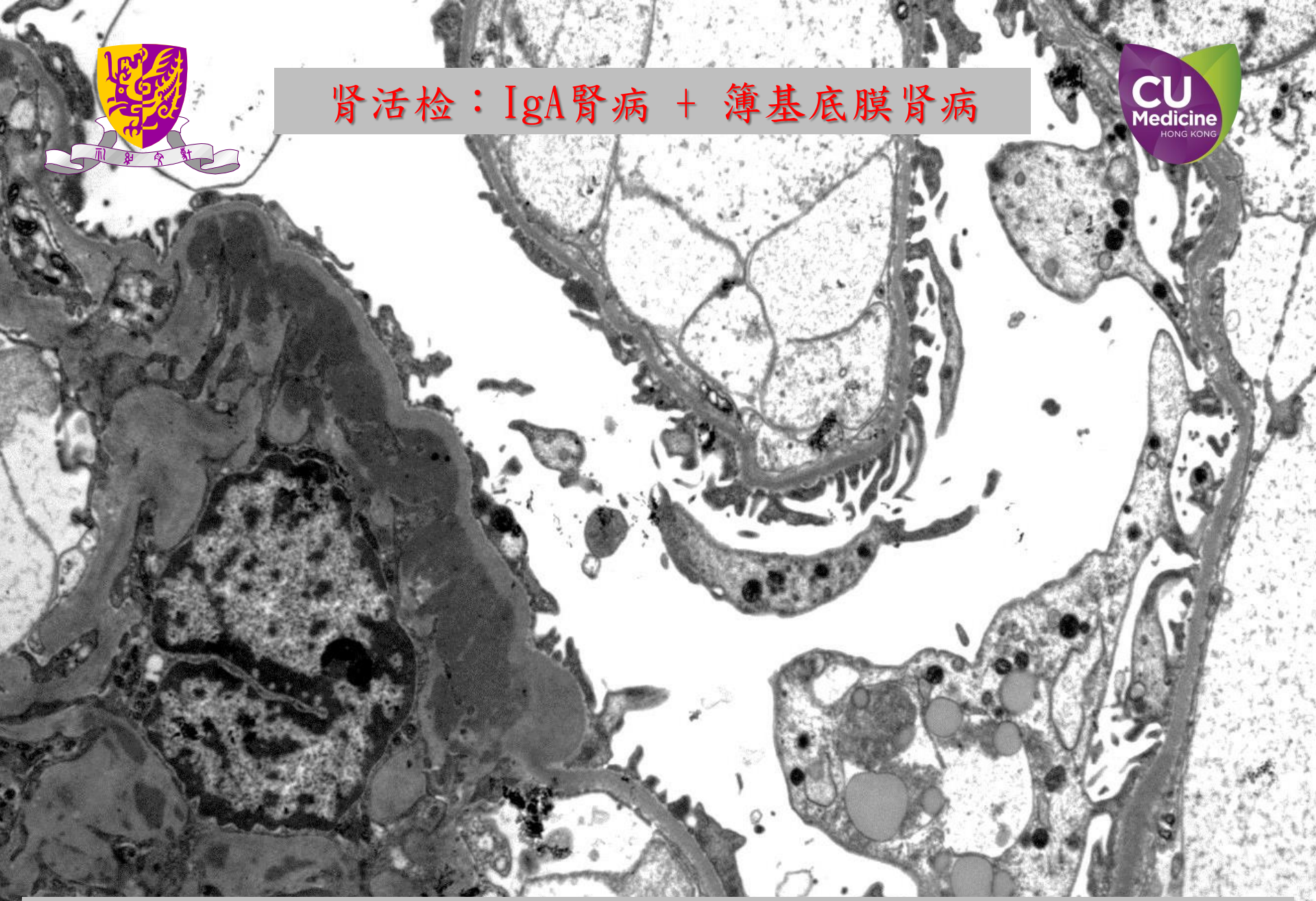
M52, renal transplant 2005, slow rise SCr 130 > 190 umol/l in 6 months, PU 0.2 g/day
Dx; No Rejection, TGCBM 14E347 GCBMT 544 ± 114 nm
F-Up: Colonoscopy one month ago, Decoy Cells + in urine, Ankylosing Spondylitis (B27+)

肾活检：IgA肾病 + 厚基底膜



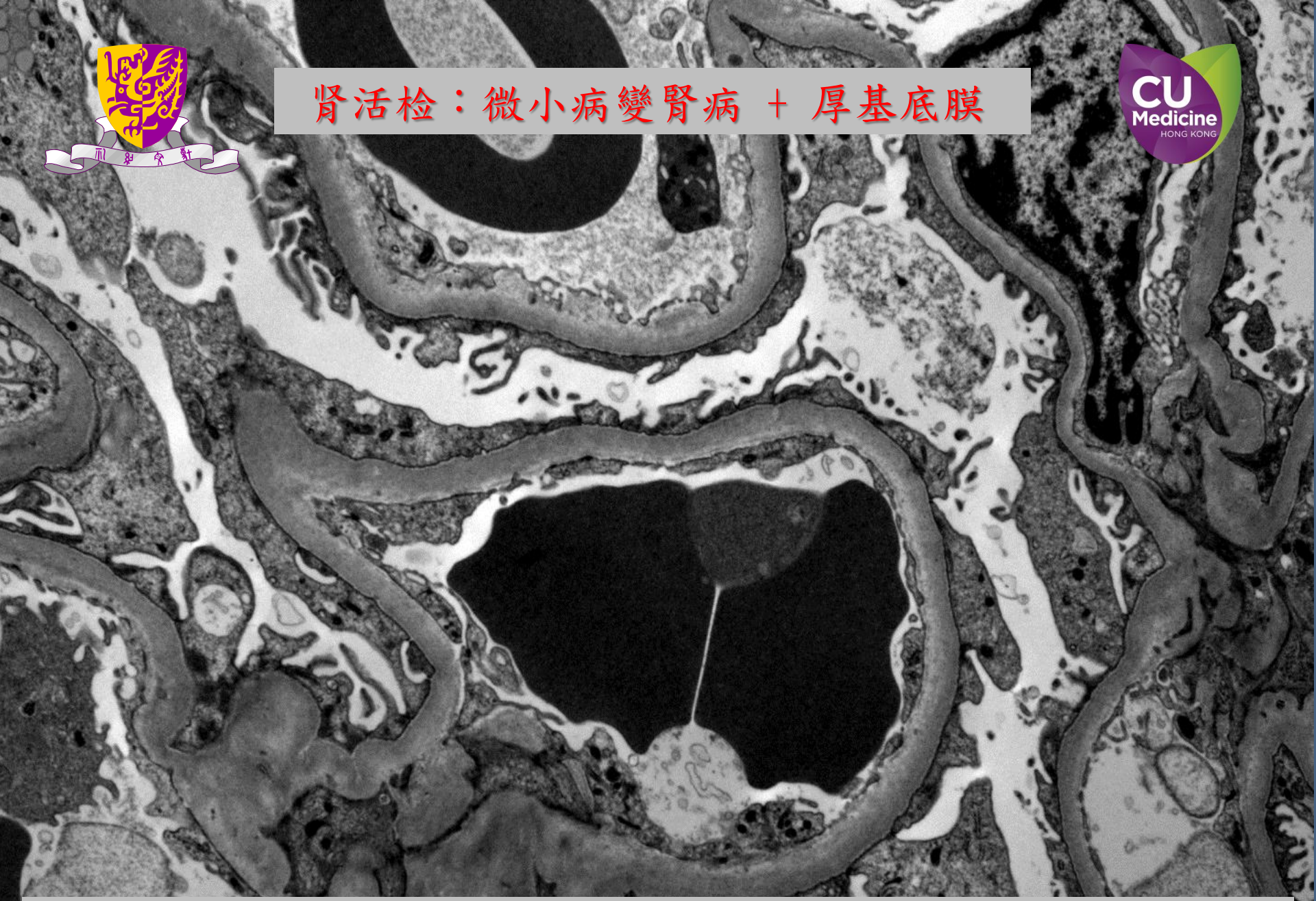
M28, recurrent gross hematuria, Scr 78 umol/l, BP 140/90 14E306 GCBMT 459 ± 102 nm
Dx; IgAN (1a,1,N) + TGCBM, Rx: ARB. F-Up 2 months: BP 140/85, 49Kg, FBG 4.7 mmol/l

肾活检：IgA肾病 + 簿基底膜肾病



F53, proteiuria, 2.1 g/day Scr 78 umol/l, 13E380 GCBMT 224 ± 49 nm Dx; IgAN I-G + TMN, Rx: ARB
F-Up 12 months: PU 0.8g/day, SCr 70umol/l, microscopic hematuria, BP 140/85

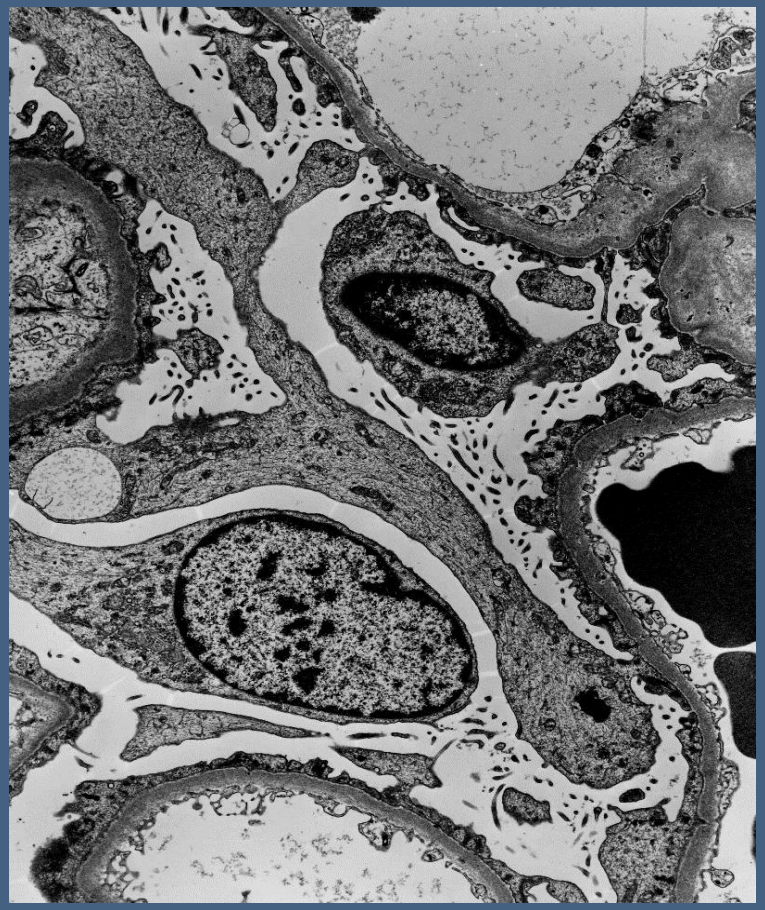
肾活检：微小病變腎病 + 厚基底膜



M36, nephrotic, 6.7 g/day Scr 67 umol/l, 13E036 GCBMT 431 ± 89 nm Dx; MCN, Rx steroids x 21 wks
F-Up 17 months: PU 0.1g/day, SCr 45umol/l, F-Up: FBG 4.3 mmol/l, HbA1C 5.7%, 75Kg/170cm/26%

MCN – from steroid sensitive to steroid resistant

從激素敏感到激素抵抗



sex/age 性別/年齡	GCBMT (nm) 基底膜厚度	months 隨訪(月)	GCBMT (nm) 基底膜厚度
F 8	**325**	56	**361**
M 4	**299**	108	**590**
M 13	**371**	67	**580**
M 10	**381**	65	**430**
M 11	**357**	75	**446**
M 10	**412**	44	**521**
M 2	**230**	112	**557**
M 3	**287**	85	**394**
M 4	**229**	96	**441**
M 5	**399**	58	**525**

MCN 5 children are resistant to steroids and became diabetic

微小病變腎病 – 五个兒童最终对激素治疗无效，並发展為糖尿病

thick GCBM 结论 – 厚基底膜肾病

临床思维和考虑 clinical aspects

chronic renal lesion, may precede diabetes

慢性肾疾病，可能先于糖尿病

lesion of the metabolic syndrome

与代谢综合征相关的病变

increasing incidence, progression?

发病率越来越高

对控制疾病的進展有潛在价值

但病变能逆转吗?

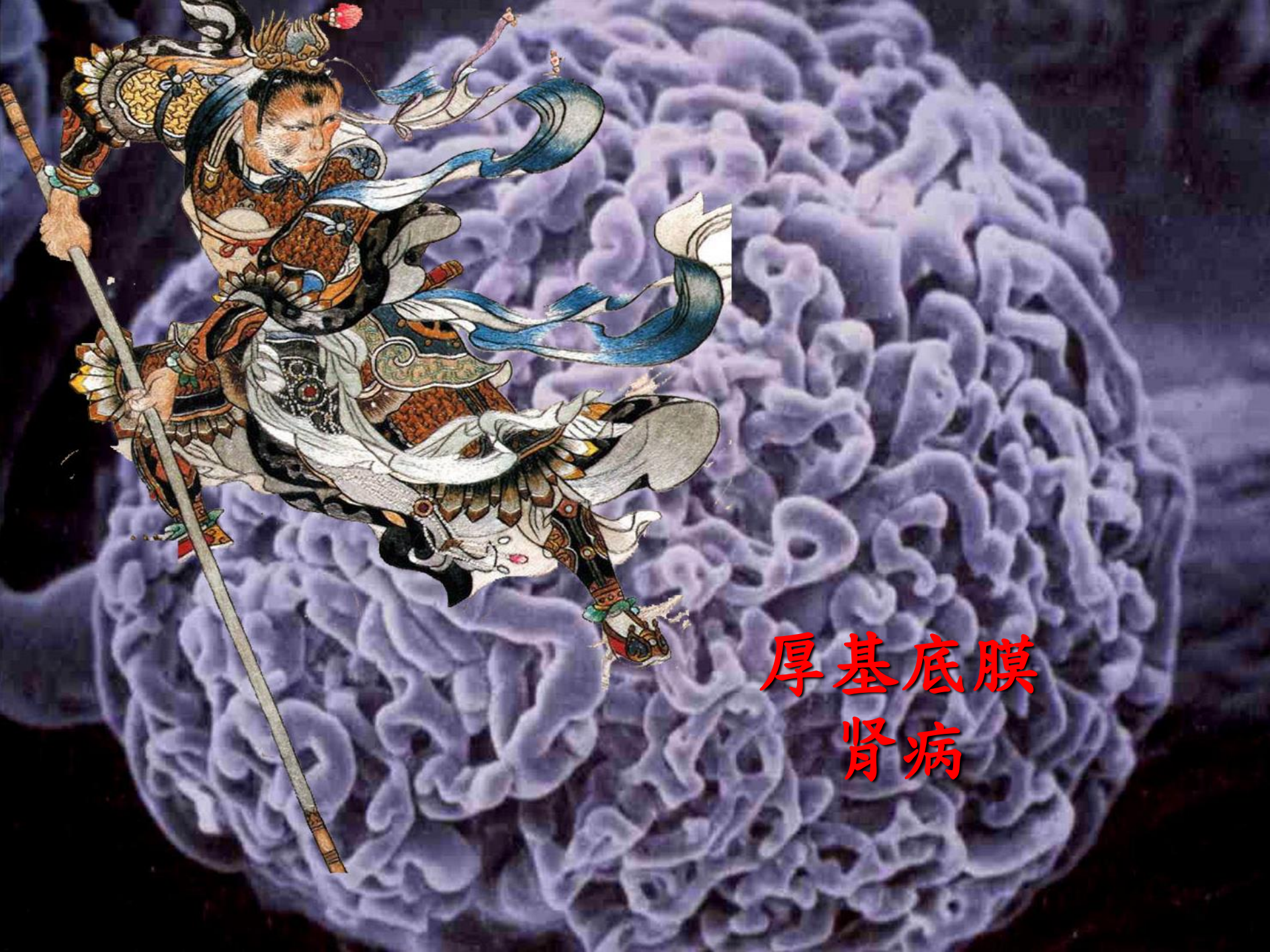
thick GCBM 结论 – 厚基底膜肾病

厚基底膜病理機制 pathogenesis

not glycemia, insulin resistance
alternate pathway – growth factors?
genetic THBS1, COX1, MMP9, COX2
不是血糖，也不仅是胰岛素抵抗，许多其他因素？

病理诊断 pathology

requires EM morphometry
may superimpose with other renal lesions
需要电镜形态
可與其他腎小球病變共存和疊加


厚基底膜
肾病