



C3G: PATHOLOGY AND UNANSWERED QUESTIONS

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Disclosure of Interests

None

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Definition of C3G

- Dominant C3 staining on IF staining
- Pattern of injury- most often membranoproliferative, followed by mesangial proliferative, rarely crescentic, with a variable degree of sclerosing lesions
- EM- Further subclassified into C3GN and DDD

Pickering, MC, D'Agati, VD, Nester, CM, Smith, RJ, Haas, M, Appel, GB, Alpers, CE, Bajema, IM, Bedrosian, C, Braun, M, Doyle, M, Fakhouri, F, Fervenza, FC, Fogo, AB, Fremeaux-Bacchi, V, Gale, DP, Goicoechea de Jorge, E, Griffin, G, Harris, CL, Holers, VM, Johnson, S, Lavin, PJ, Medjeral-Thomas, N, Paul Morgan, B, Nast, CC, Noel, L-H, Peters, DK, Rodriguez de Cordoba, S, Servais, A, Sethi, S, Song, W-C, Tamburini, P, Thurman, JM, Zavros, M, Cook, HT: C3 glomerulopathy: consensus report. *Kidney Int*, 84: 1079-1089, 2013.

Can we do more with the biopsy

- Confirmation of alternative pathway of complement activation versus role for other complement pathways (classical and lectin): Role for C4d staining

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Sethi, S, Nasr, SH, De Vriese, AS, Fervenza, FC: C4d as a Diagnostic Tool in Proliferative GN. *Journal of the American Society of Nephrology*, 26: 2852-2859, 2015.

Can we do more with the biopsy

- Pronase studies to determine whether unmasked deposits are present- in particular monotypic Ig deposits

Larsen, CP, Messias, NC, Walker, PD, Fidler, ME, Cornell, LD, Hernandez, LH, Alexander, MP, Sethi, S, Nasr, SH: Membranoproliferative glomerulonephritis with masked monotypic immunoglobulin deposits. *Kidney Int*, 88: 867-873, 2015.

Can we do more with the biopsy

- Electron microscopy: Overlap of C3GN and DDD findings- does it matter?

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<http://www.kidney-international.org>

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**Overlap of ultrastructural findings
in C3 glomerulonephritis and
dense deposit disease**

C3 or more than C3

- Breakdown/activation products of C3: convincing mass spectrometry data
- Staining for C5-9

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Other pathology questions-Patterns of injury

- Rare cases of severe crescentic C3G, sclerosing lesions
- Substructures in C3G deposits

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Post infectious GN and C3GN: can we/should we separate the two

- Clinical presentation/duration of kidney disease
- Pattern- diffuse proliferative GN
- Presence of IgG + C3 versus C3 only
- Subepithelial humps
- Ancillary studies- C4d

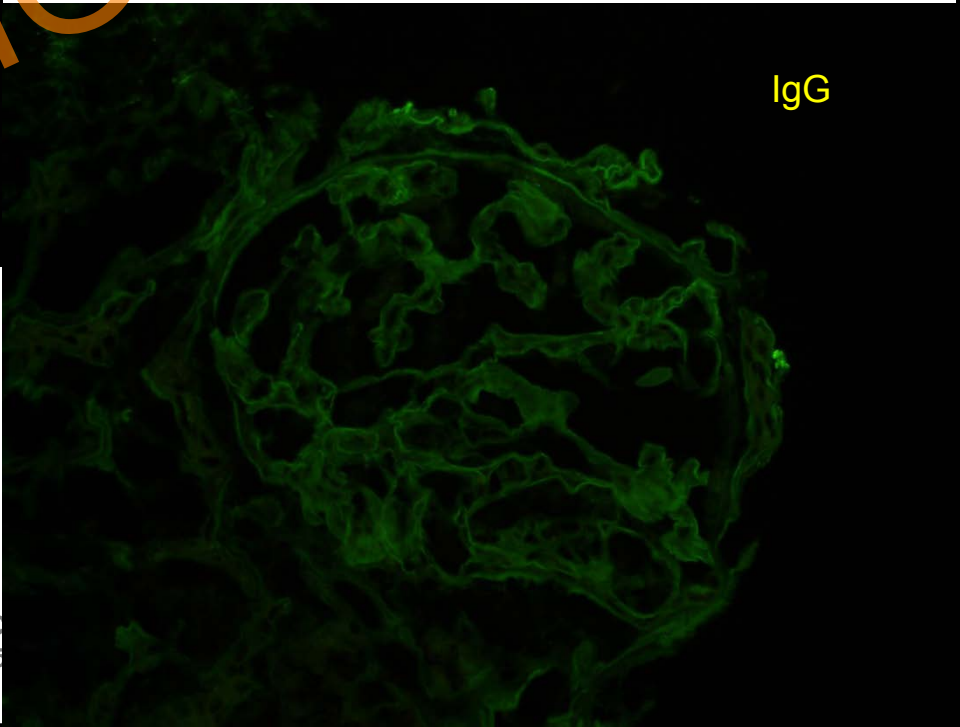
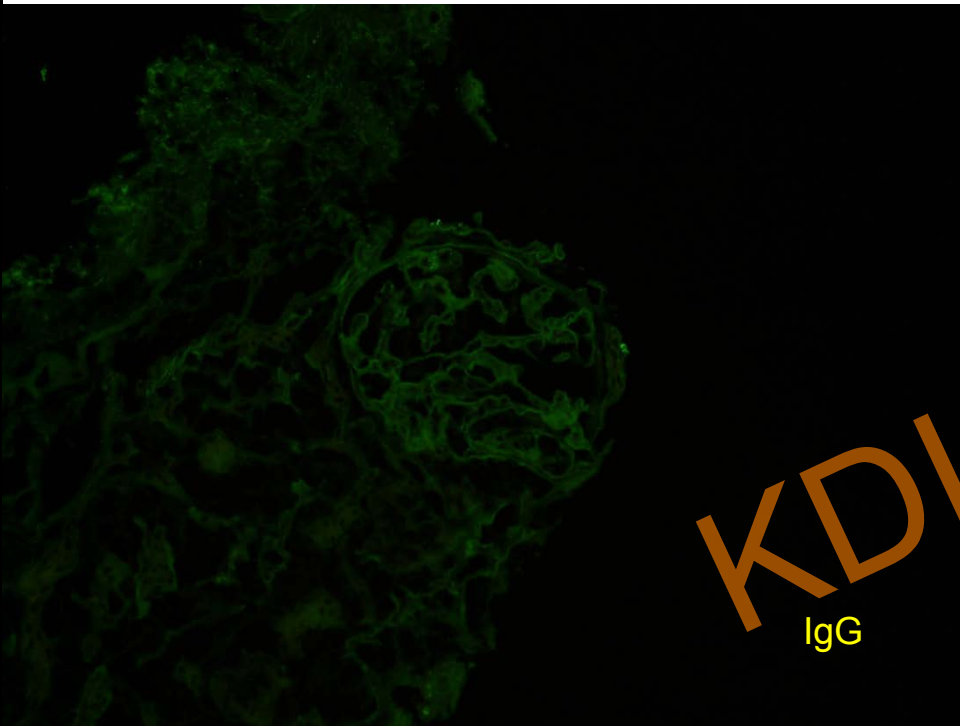
Thank you

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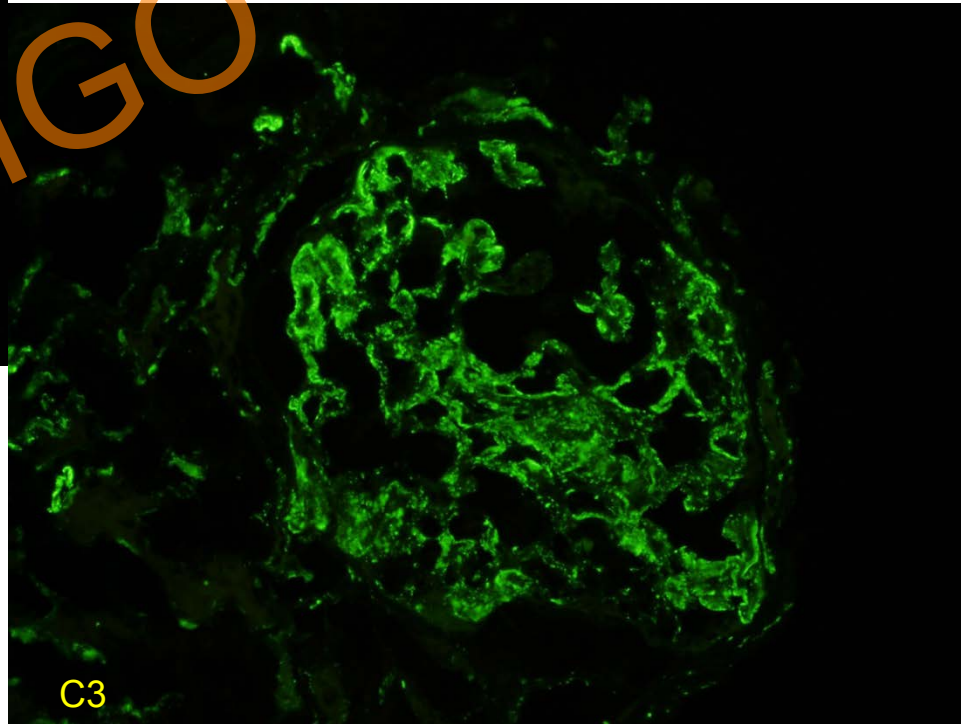
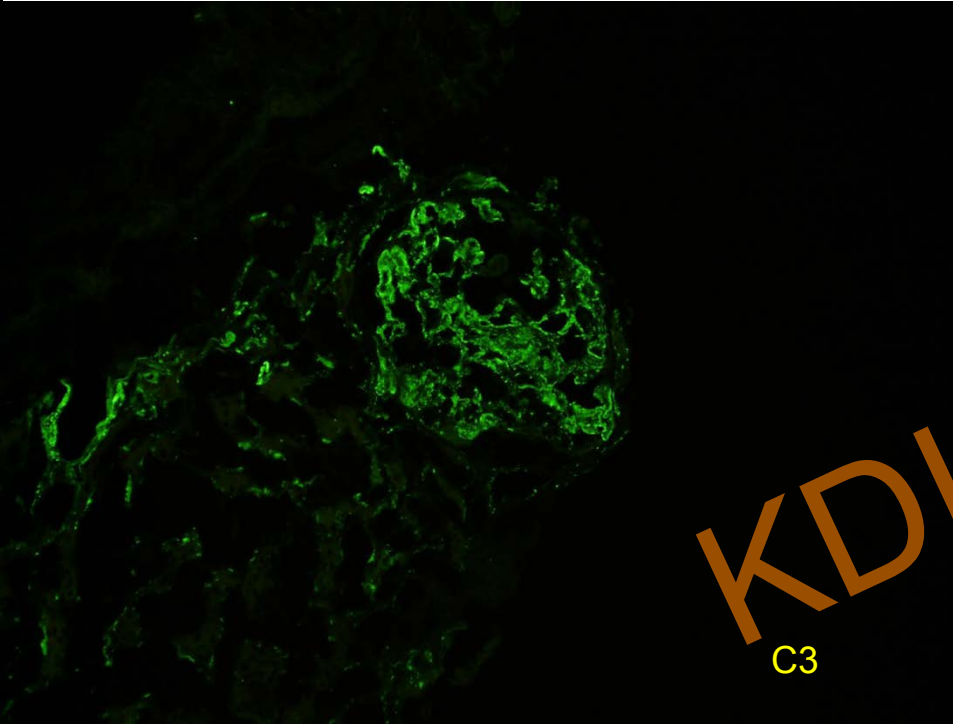
*KDIGO Controversies Conference on Complement-Mediated Kidney Diseases
November 19-21, 2015 | Barcelona, Spain*



Recurrent C3GN-role for C4d

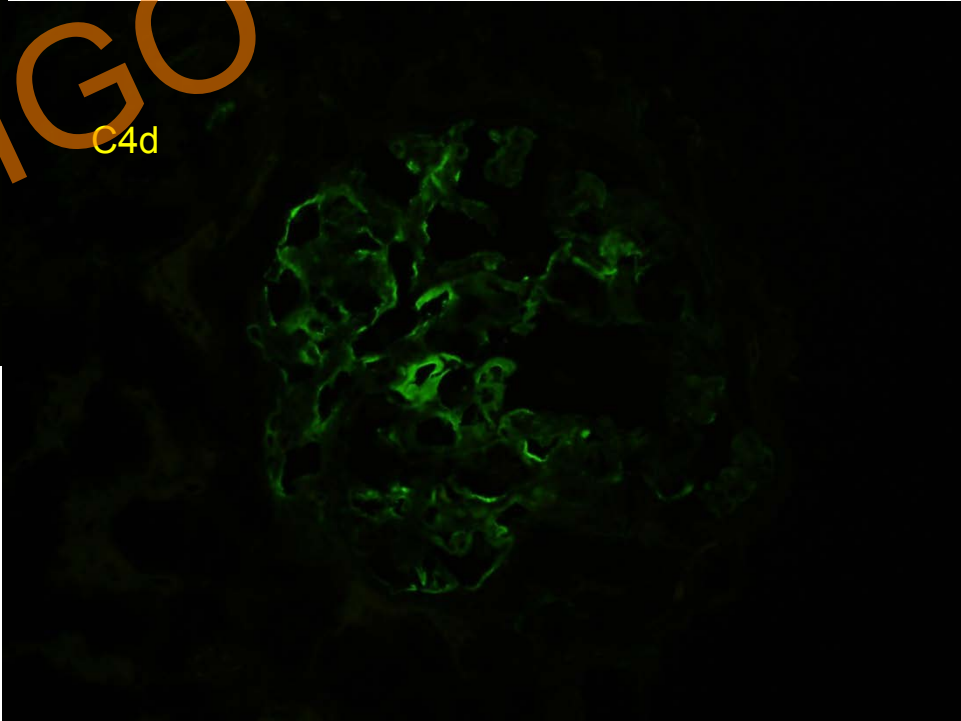
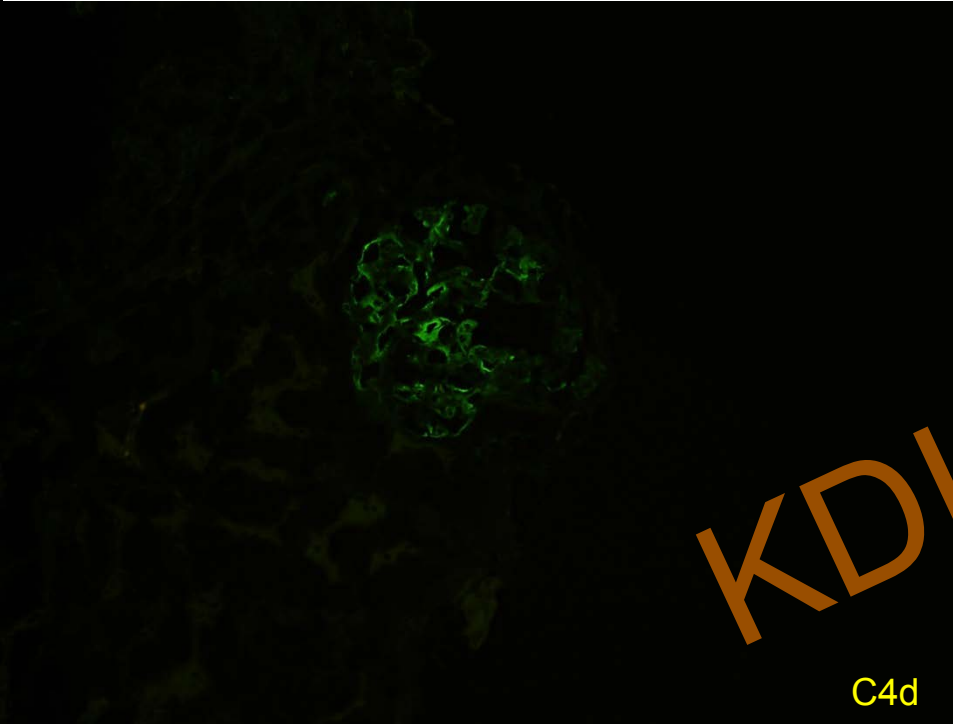


C3 in recurrent C3GN



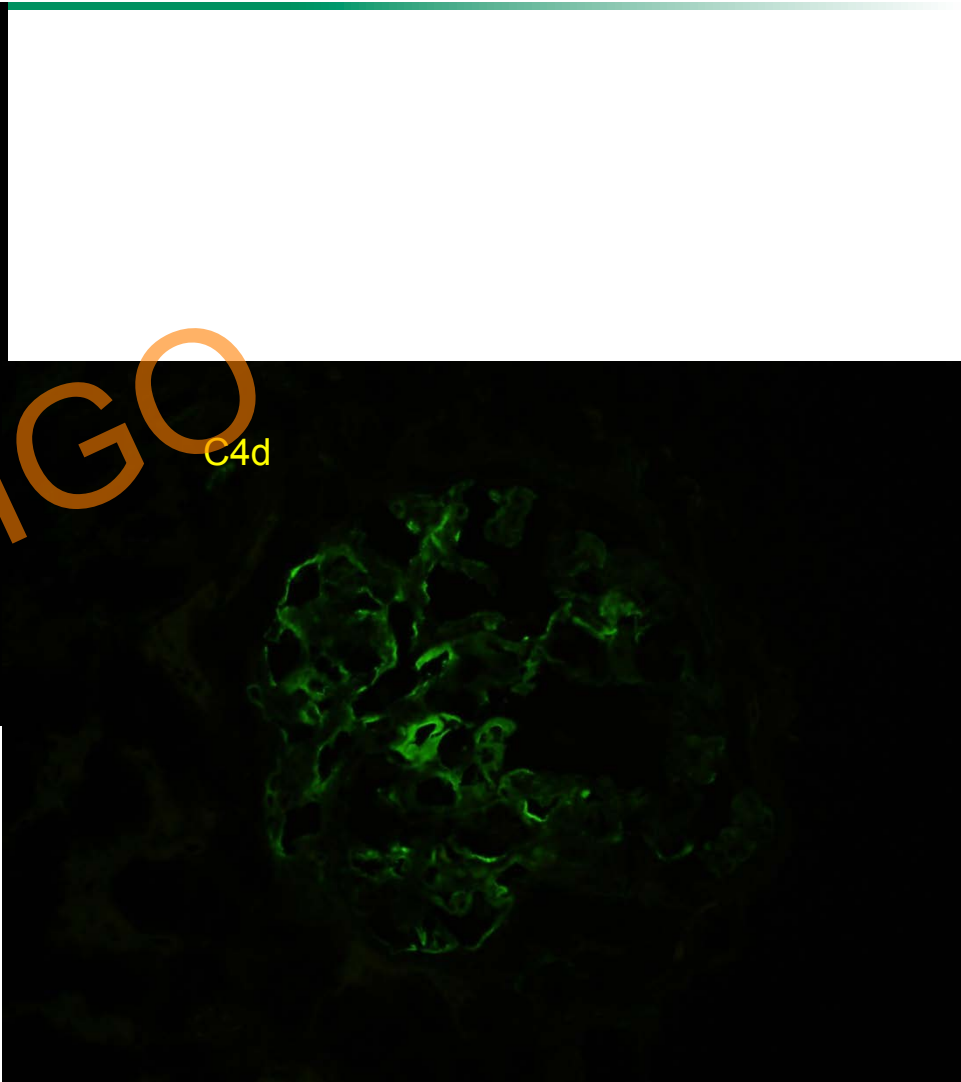
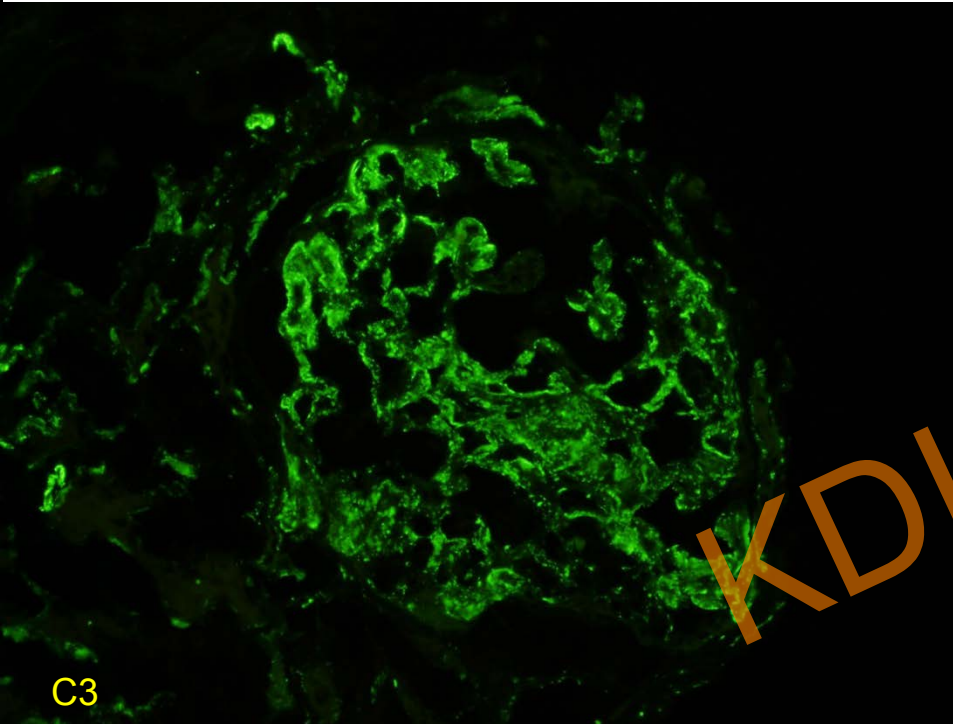
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C4d

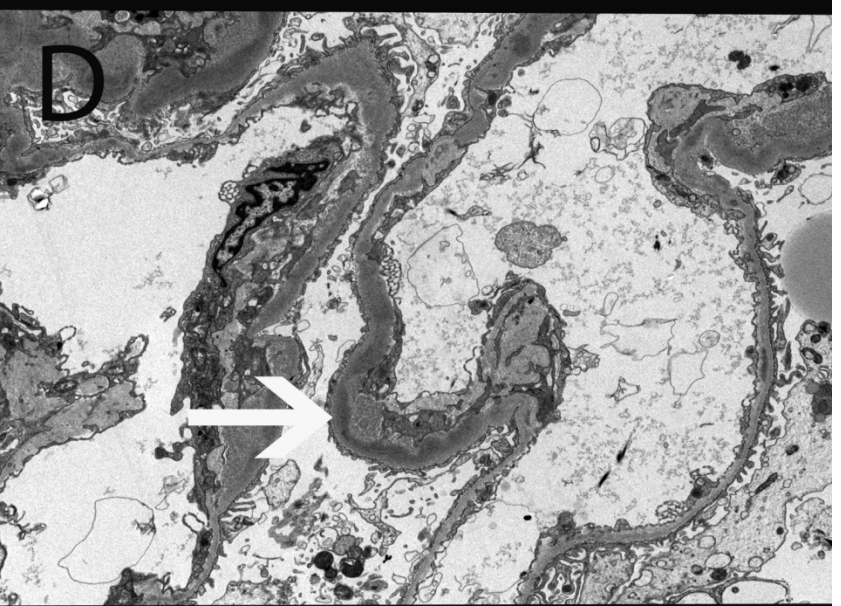
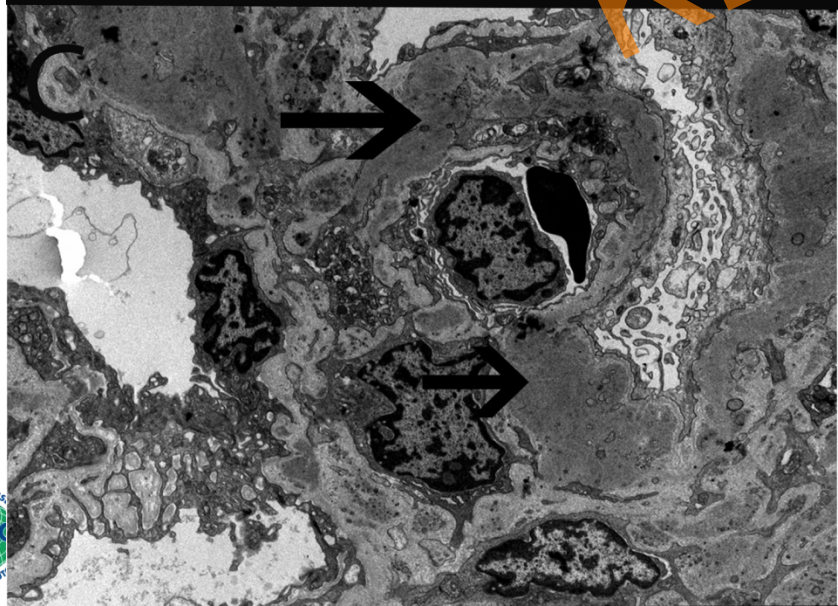
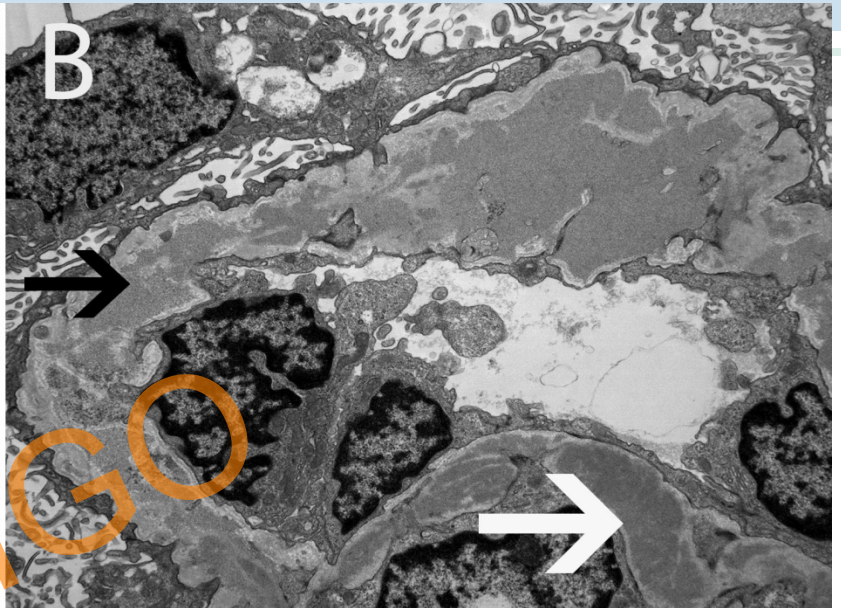
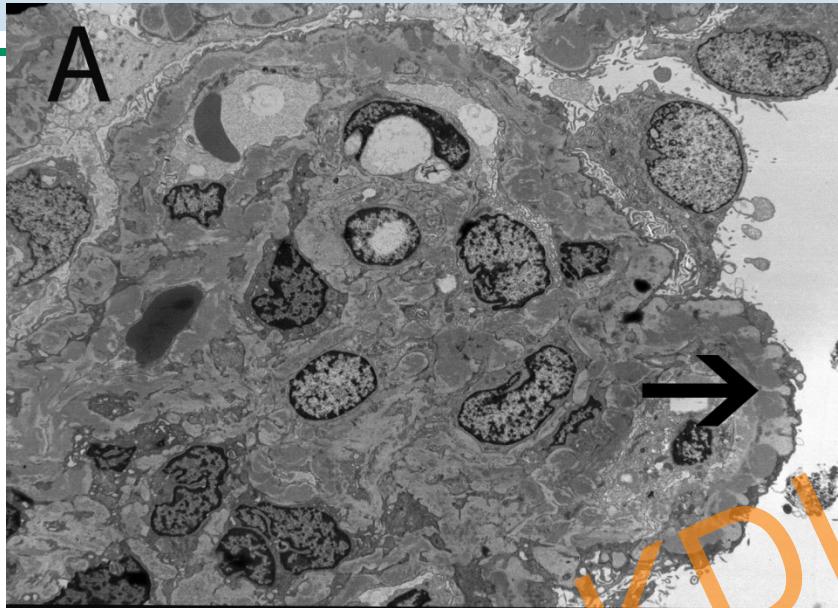


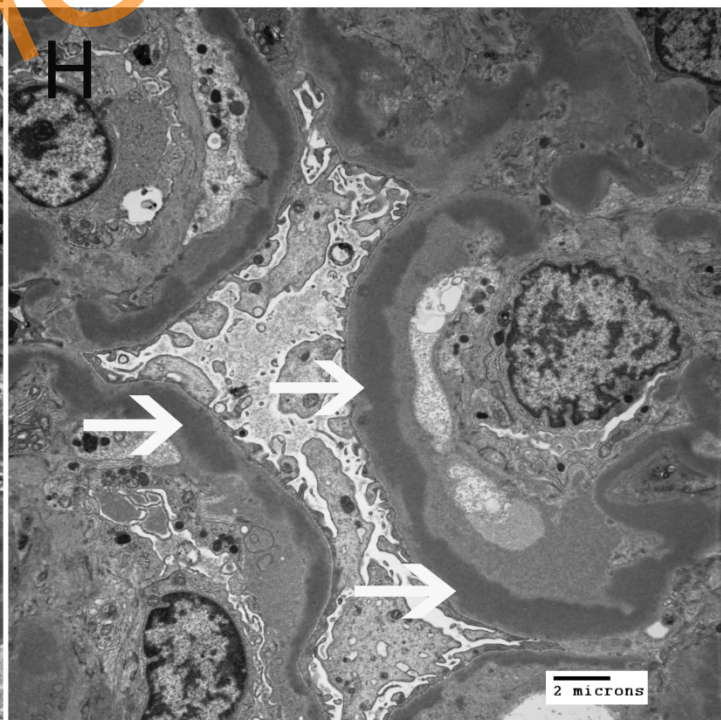
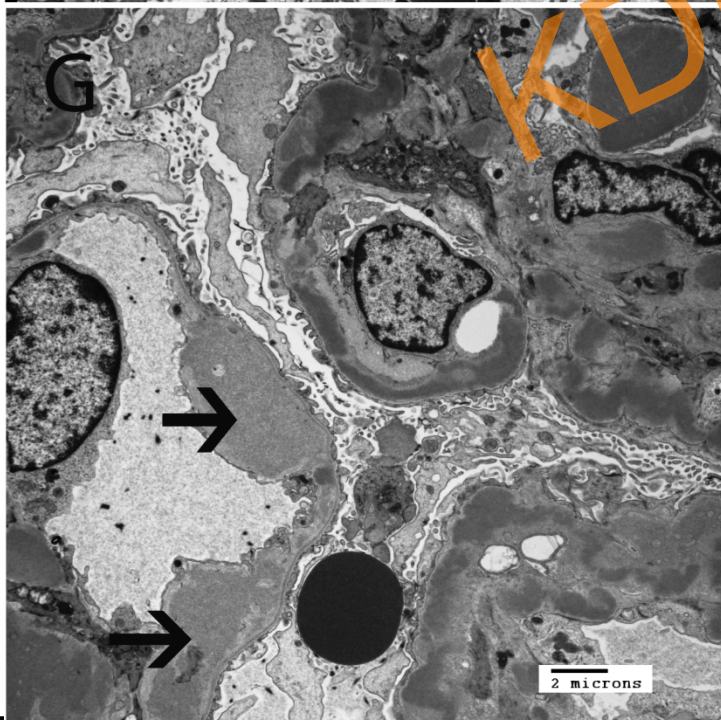
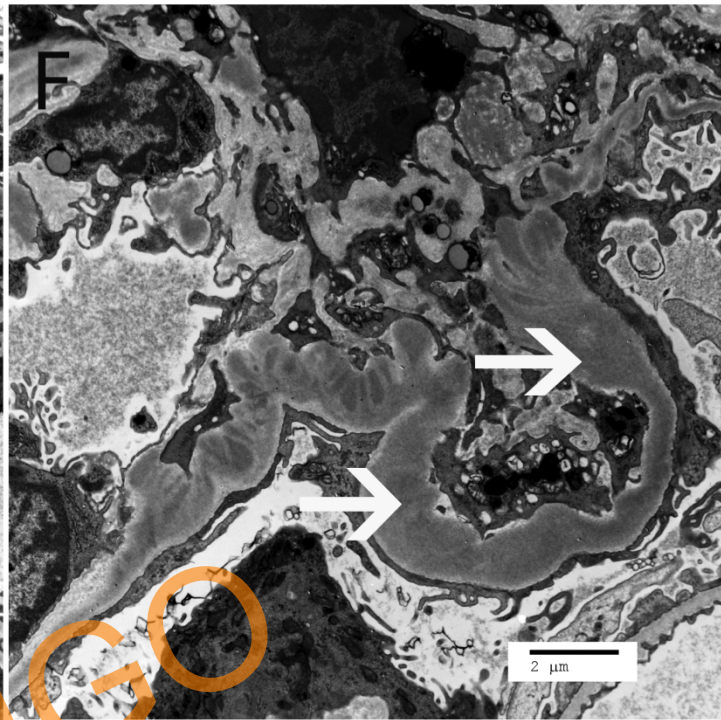
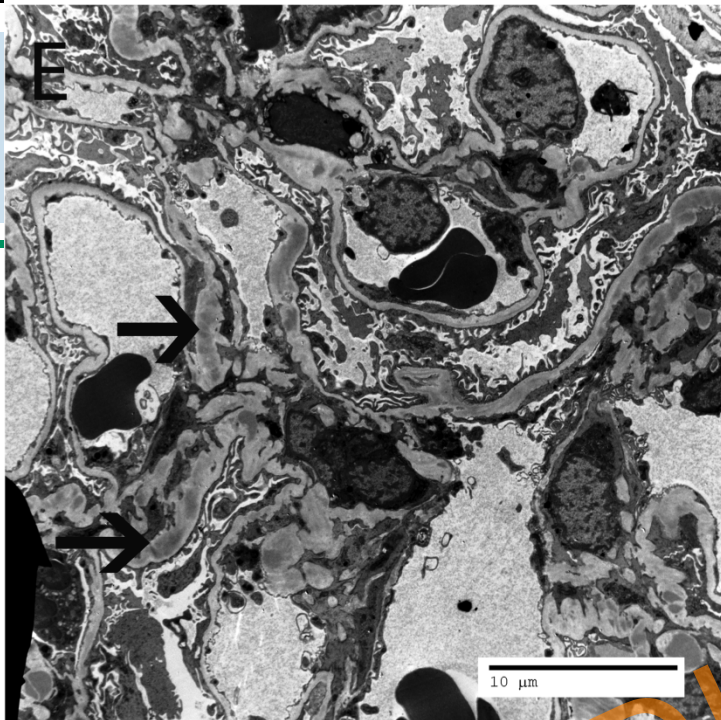
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C3 versus C4d

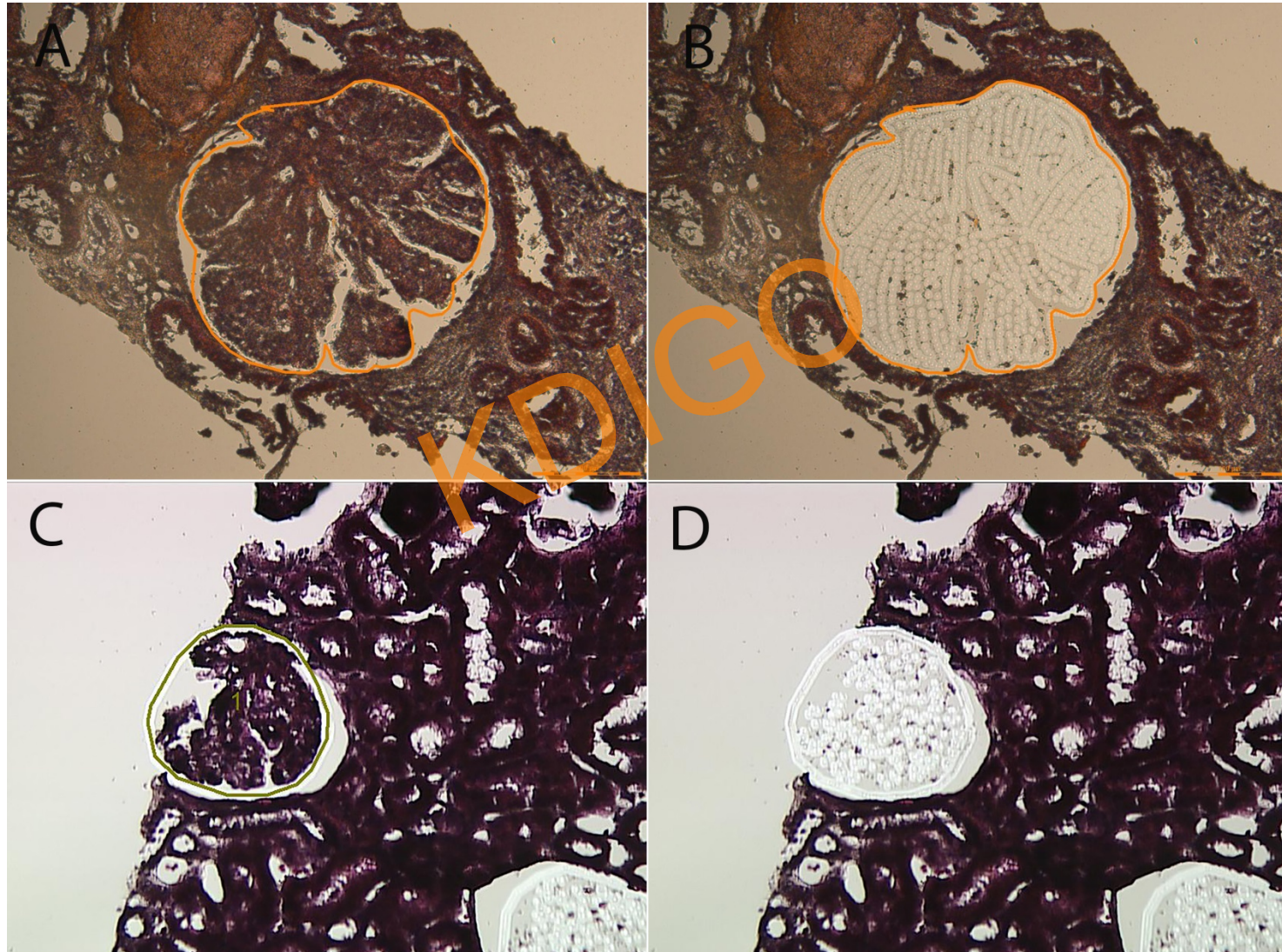


Overlapping features





Breakdown/activation products of C3



LCMS of 6 patients of C3GN and 6 patients of DDD

#	Starred Bio View: Identified Proteins (14/1395)	Probability Legend:											
		Patient 01	Patient 02	Patient 03	Patient 04	Patient 05	Patient 06	Patient 07	Patient 08	Patient 09	Patient 10	Patient 11	Patient 12
1	★ Complement C3	71	44	79	10	15	21	75	24	8	7	25	22
2	★ Complement factor H-related protein 1	22	5	16	3	2	7	19	11	4	3	7	5
3	★ Complement component C9	21	15	17	7	4	4	14	6		4	2	3
4	★ Complement C5	16	7	13	4	4	6	16	2		2	6	7
5	★ Complement factor H-related protein 5	11	7	3			1	2	3			1	3
6	★ Complement component C8 alpha chain	5	2	9	1	1	1	6	2			1	2
7	★ Complement component C6	5	4	5	2	2	2	3	3		2		2
8	★ Complement component C8 beta chain	6	3	5	1	2	2	3	2		1		1
9	★ Complement component C7	6	2	5	1			5					3
10	★ Complement component C8 gamma chain	3	2	4	1	1	2	2			1		
11	★ Complement C4-A	3			1	1							2
12	★ Complement factor H-related protein 2	4		2				2					
13	★ Complement factor H	7		1									1
14	★ Complement factor I								1			1	

C3 glomerulonephritis

CO3_HUMAN (100%), 187,149.1 Da
 Complement C3
 27 unique peptides, 35 unique spectra, 79 total spectra, 329/1663 amino acids (19% coverage)

MGPTSGPSLL LLLLTHLPLA LGSPMYSIIT PNILRLESEE TMVLEAHDAQ GDVPVTVTVH DFPGKKLVLS SEKTVLTPAT
 NHMGNVTFTI PANREFKSEK GRNKFVYQA LFTGTQVVEKV VLVSLQSGYL FIQTDKTIYT PGSTVLYRIF TVNHKLLPVG
 RTVMVNIENP EGIPVKQDSL SSQNQLQNP LSWDIPPELVN MGQWKIRAYY ENSPOQVVFST EFEEVKEYVLP SFEVIVEPTE
 KFYIYNEKG LEVITITARFL YGKRKVEGAF VYFGIQDGEQ RISLPESLKR IPIEDGSGEV VLSRKVLLDG VQNPRAEDLV
 GKSLEYVSATV ILHSGSDMVQ AERSGIFVYI SPYQIHFTKT PKYFKPGMPF DLMVFTVTPD GSPAYRVPVA VGGDTVQSL
 TOGDGVAKLS INTHPSQKPL SITVTRVDE LSEAEQATR MQALPYSTVG NSNNYLHLSV LRTELRPGET LNVEFLLRMD
 RAHEAKIRYY TYLIMNKGRL LKAGRQVPEP QDDLVLVPLS ITTDFIPSEF LVAYYTLIGA SGQREVVADS VWVFKDSCV
 GSLVVKSGQS EDRQPVVPGQQ MTLKIEGEG ARVVLVAVDK GVFLNKKNK LTQSKIWDVV EKADIGCTPG SGKLYAGVFS
 DAGLTFSSS GQTAQRAEL QCQPAAARRR RISVQLTEKRM DKYVGKYPKEL RKCCEDGMRE NPMRFSCQRR TRFSLGEAC
 KKVFLDCCNY ITELRRQHAR ASHGLLARISN LDEDIIEEN IYSRSEFPES WLNWVEDLKE PPKNGISTKL MNIKZKDSIT
 TWEILAVSMS DKKGICVADP FEYIVMQDFE IDLRLPYSVV RNEQVEIRAV LYNRYRQNEL KVRVELLHNP AFCSLATTKR
 RHQQTVTIPP KSSLSVPPYVI VPKLSTGLQEV EVKAAVYHFF ISDGRKSLK VVPEGIRMNK TVAVRTLDP ERLGRLEGVQKE
 DIPPADLSDQ VPDTESETRI LLAGTPVAQM TEDAVDAERL KHLIVTSPGC GEQNMIGMTP TVIAVHYLDE TEQWEKFGLE
 KRQGALSLIK KGYTQQLAFR QPSAFAAFV KRAPSTWLTAY VYKYFESLAV NLIAIDSQVL CGAVKWLILE KQKPDGVFQE
 DAPVIHQEMI GGLRNNNEKD MAFAFVLIS LQEAKDICEE QVNSLPGSIT KAGDFLEANY MNLQRSYTV A IAGYALAQMG
 RLKGPLLNKF LTTAKDKNRW EDPSGKQLYNV EATSYALLAL LQLKDFDFVP PVVRWLNEQR YYGGGYGSTQ ATFMVFAQALA
 QYQKDAPDHQ ELNLDVSLQL PSRISKITHR IHWESASLLR SEETKENEGF TVTAEGKGGQ TLSVVTMYHA KAKDQLTCNK
 FDLKVTIKPA PETEKRPQDA KNTMILEICT RYRQDQDATM SILDISMMTG FAPD TDDLKQ LANGVDRYIS KYELDKAFSD
 RNTLIIYLDK VSHSEDDCLA FKVHQYFNVE LIQPGAVKVV AYNLEESC T RFYHPEKEDG KLNKLCRDEL CRCAEENCFI
 QKSDDKVTL ERLDKACEPG VDYVYKTRLV KVQLSNDFDE YIMAEQTIK SSGDEVQVGG QRTFISPIKC REALKLEEKK
 HYLMWGLSSD FWGKPNLSY IIGKDTWVEH WPEEDECCDE ENQKQCQDLG AFTESMVVFG CPN

Location of bars

- Before red bar: Signal sequence
- Between two red bars = β chain
- Between two black bars = C3a
- Between second black and first blue = C3c ($\alpha 1$)
- Between blue bars = C3dg
- Between second blue to green bar = C3f
- From green to end = C3c ($\alpha 2$)



4B. Dense deposit disease

CO3_HUMAN (100%), 187,149.1 Da

Complement C3

18 unique peptides, 24 unique spectra, 25 total spectra, 211/1663 amino acids (15% coverage)

MGPTSLPSSL	LLLLTHLPLA	LGSPMYSIIT	PNILRLESEE	TMVLEAHDAQ	GDPVPTVTVH	DFPGKKLVLS	SEKTVLTPAT
NHMGNTFTI	PANREFKSEK	GRNKFTVQA	TEGTQVVEKV	VLVSLQSGYL	FIQTDKTIYT	PGSTVLYRIF	TVNHKLLPVG
R TVMVNIENP	EGIPVK QDSL	SSQNQLVLP	LWDIPELVN	MGQWKIRAYY	ENSPQQVFS	EFEVKEYVLP	SFEVIVEPTE
KFYIYNEKG	LEVITITARFL	YGKKVEE	VDFGIQDGEQ	RISLPESLKR	IPIEDGSGEV	VLSRKVLLDG	VQNPR AEDLV
GKSLYVSATV	ILHSGSDMVQ	AERSGI	SYQIHFTKT	PKYFKPGMPF	DLMVFVTNPD	GSPAYR VPVA	VQGEDTVQSL
TQGDGVAK LS	INTHPSQKPL	SITVRT	LEAEQATRT	MQUALPYSTVG	NSNNYLHLSV	LRTELRPGET	LNV FLLRMD
RAHEAKIRYY	TYLIMNKGRL	LKAGR	LDLVVLP	ITDFIPSPF	LVAYYTLIGA	SGQREVVADS	VWV VKDSCV
GSLVVKSGQS	EDRQPVPGQQ	MTLKI	AVVAVAVDK	GVFVLNKKNK	LTQSKIWDVV	EKADIGCTPG	SGK YAGVFS
DAGLTFSSS	GQQTAAQRAEL	QCPQPA	RSVQLTEKRM	DKVGGYRPEL	RKCCEDGMRE	NPMRFSCQR	TRF SLGEAC
KKVFLDCCNY	ITELRRQHAR	ASHLGLARSN	LDEDIAEEN	IYSRSEPPES	WLWNVEDLKE	PPKNGISTKL	MNI LKDSIT
TWEILAVSMS	DKKGCVADP	FETVMQDFF	IDLRLPYSVV	RNEQVEIRAV	LYNYRQNQEL	KVRVELLHNP	AFC LATTR
RHQQTVTIPP	KSSLSVPYVI	VPK TGLQEV	EVK AAVYHFF	ISDGVKSLK	VYPEGIRMNK	TVAVRTLDP	RLGREGVQK E
DIPPADLSDQ	VPDTESETRI	LLGTPVAQM	TEDA VAERL	KHLIVTPSGC	GEQNMIGMTP	TVI AVHYLDE	TEQWEK FGLE
KR QGALELIK	KGYTQQLAFR	QPSAFAAFV	KRAP STWLTA	YVVKYFSLAV	NLIAIDSQVL	CGAVKWLILE	K QKPDGVFQE
DAPVIHQEMI	GGLRNNNEKD	MA TAFVLIS	LOEAK DICEE	QVNSL PGSIT	KAGDFLEANY	MNLQR SYTVA	IAGYALAQM G
RLKGPLLNKF	LTTAKDKNRW	ED SKOLYNV	EATSY ALLAL	LQLKDFDFVP	PVVRWLNEQR	YGGGGYGSTQ	ATFMV FQALA
QYQKDAPDHQ	ELNLDVSLQL	PSRSSKITHR	JHWES ASLLR	SEETKENEGF	TVTAEGKGGQ	TLSVVTMYHA	KAKDQ LTCNK
FDLKVTIKPA	PETEKRPQDA	KNTMILEICT	RYRGDQDATM	SILDISMMTG	FAPD TDLLKQ	LANGVDRIYS	KYELDKAF SD
RNTLIYLDK	VSHSEDDCLA	FKVHQYFNVE	LIQ P GAVKVY	AYYNEESCT	RFYHPEKEDG	KLNKL CRDEL	CRCAEEN CFI
QKSDDKVTLE	ERLDKACEPG	VDYVYKTRLV	KVQL S NDFDE	YIMAIEQTIK	SGSDEVQVGO	QRTFI SPIKC	REALK LEEKK
HYLMWGLSSD	FWGKEPNLSY	IIGKDTWVEH	WPEEDECQDE	ENQKQCQDLG	AFTESMVVFG	CPN	

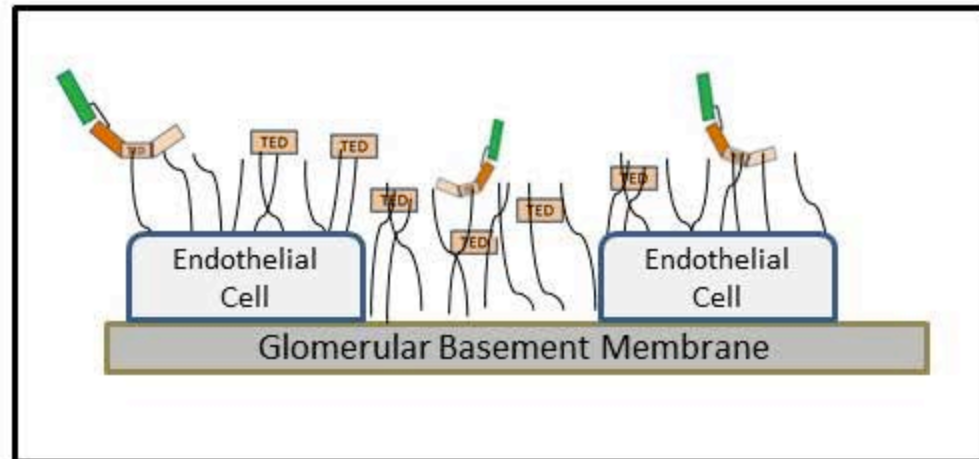
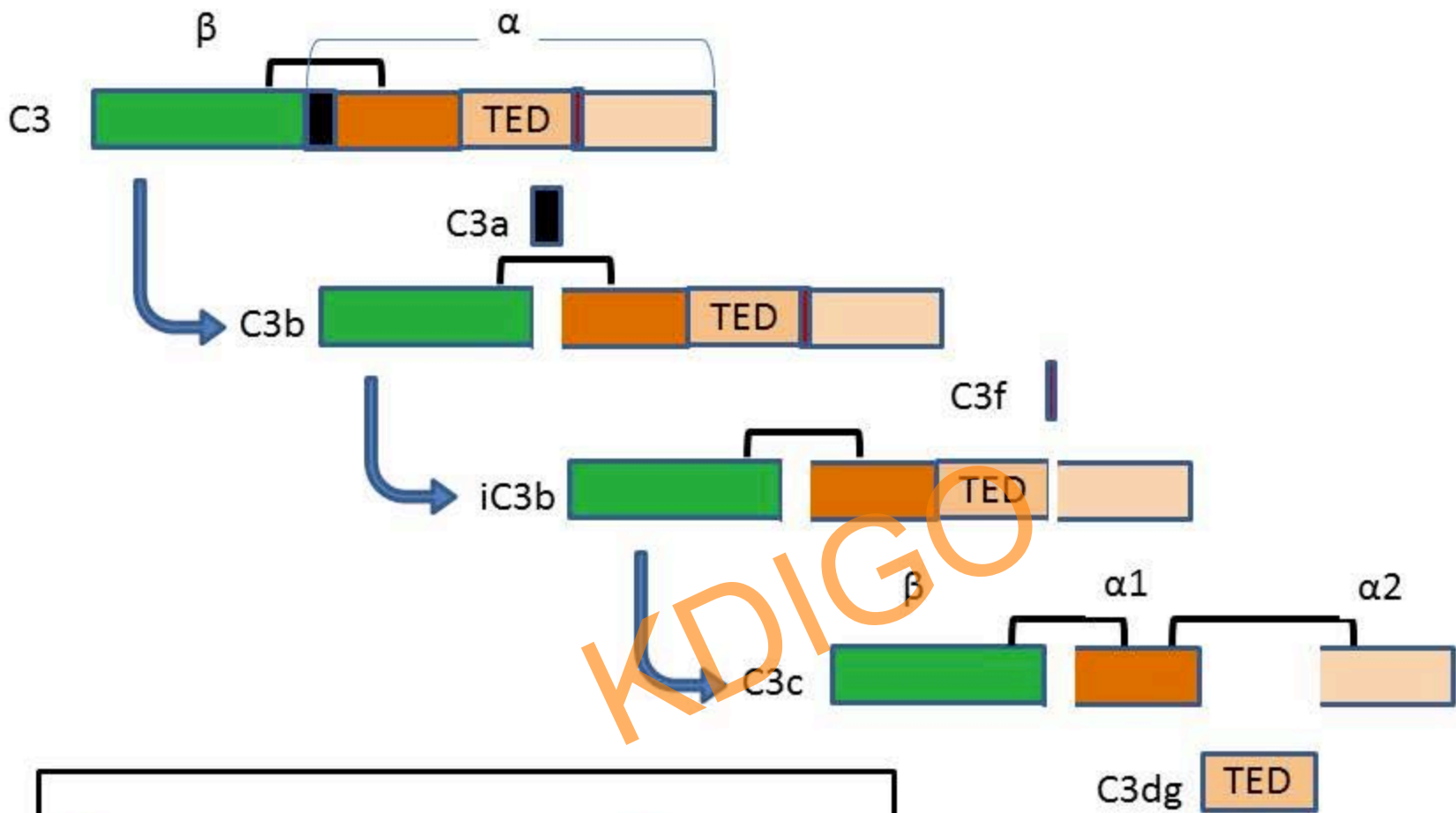
Complement C3

All Biological Samples

Sequence Coverage	Protein	Accession	Bio Sample	Prob	%Spec	#Pep	#Uni...	#Spec	%Cov
	Complem...	CO3_HUM...	Patient 01	100%	1.1%	26	36	75	18%
	Complem...	CO3_HUM...	Patient 02	100%	0.085%	3	3	5	2.3%
	Complem...	CO3_HUM...	Patient 03	100%	0.066%	3	3	4	2.2%
	Complem...	CO3_HUM...	Patient 04	100%	0.22%	10	12	12	9.0%
	Complem...	CO3_HUM...	Patient 05	100%	0.28%	12	14	15	9.9%
	Complem...	CO3_HUM...	Patient 06	100%	0.50%	15	21	24	13%
	Complem...	CO3_HUM...	Patient 07	100%	1.00%	32	40	77	23%
	Complem...	CO3_HUM...	Patient 08	100%	0.41%	10	12	26	7.3%
	Complem...	CO3_HUM...	Patient 09	100%	0.10%	6	6	8	4.3%
	Complem...	CO3_HUM...	Patient 10	100%	0.14%	5	7	7	5.1%
	Complem...	CO3_HUM...	Patient 11	100%	0.53%	19	26	28	16%
	Complem...	CO3_HUM...	Patient 12	100%	0.43%	13	19	23	11%

Percentage amino acid coverage of C3 proteins detected by mass spectrometry

		Overall amino acid coverage	C3 β chain	C3a	C3c- α 1	C3dg	C3f	C3c- α 2
Patient 1	C3GN #1	16	6.3	0	4.3	30.9	0	7.0
Patient 2	C3GN #2	16	11.5	0	4.3	35.5	0	17.5
Patient 3	C3GN #3	19	17.8	0	12.1	34.6	0	17.7
Patient 4	DDD #1	8	2.2	0	14.5	24	0	3.5
Patient 5	DDD #2	10	10	0	0	23.2	0	3.5
Patient 6	DDD #3	11	7.7	0	4.3	30	0	3.5
Patient 7	C3GN #4	23	16	0	14.5	50	0	17.7
Patient 8	C3GN #5	7	0	0	0	30	0	0
Patient 9	C3GN #6	4	0	0	0	16.9	0	3.5
Patient 10	DDD #4	5	0	0	14.5	15.4	0	0
Patient 11	DDD #5	15	9.3	0	4.3	47	0	3.5
Patient 12	DDD #6	10	5.9	0	4.3	32	0	0



C5b-9 staining

Supplement: C3 coverage map showing number of unique peptides, number of total spectra and number of unique spectra

Patient 1

C3

C03_HUMAN (100%), 187,149.1 Da
Complement C3
23 unique peptides, 33 unique spectra, 71 total spectra, 265,1663 amino acids (16% coverage)

```

MDFSTGSPSLL LLLLETHPLA LQSPMYSIIT PNILRLSEEE TMVLEAHDAQ GDVFPVTVYH DFFGKKLVLS SEKTVLTPAT
NHMGNVFTFI PANREFKSEK GRNKFTVGA TFQGVVEVK VLVLSOSGYL FIQDKTIYT PGSTVLYRIF TVNHKLLPVG
RFTVMVNIENP KGIIVKQDSSL SSQNLQVLPL LSWDIPRLVN MQQWIRAVY EHSPOQVFSY EFKVKEYVLP SFVEVIVEPTE
KFFYIYNEHG LEVITARFL YDKKVEGAF VIFQIQDGE RLSLPESLHR IPIEDQGEV WLNKVLIDG VQNPRAEDLV
GKSLVVSATV ILHSGSDMV AERSOIPVTV SPYQIHFTKT PKYFKPGMPF OLMVFTVNPD GSPAYRVPVA VOGEDTVQSL
TQDQGVAKLS INTHPSSKPL SITVETKKEE LSEAEQATR MGALPYSTVG NSNNYLHLSSV LRTELRPGET LNVNFFLRMD
RAHEAHRVY TYLIMNKRGL LEAGRTVSRG OGDVLRISFR ITDIFLPSFR LVAYTLIOA EKADIQCTPD SOKDYAGVRS
GSLVHSSQS EDRQPPGQO MTLKIEGDH ARVVLVAVDK OVFLNKKNK LTOSKIWDVV EKADIQCTPD SOKDYAGVRS
DAQLTFTSS GQGTAPRAEL GQPPAPARR RSVQLTEKRM DAVGKYPREL KCCGEDMRE NPMRFSQDR TRFISLGEAC
KRVFLDCCNY ITELRRGHAR ASHLGLARSN LDEOIAEEN IVSRSEFFES WLWNVEDLKE PPKNGI STL MNIFLKDSIT
TWEI LAVSMS DKKGICVADP FEVTVMDFF IDLRLPYSVV IDDVVRKSLK VVPEQIRMNK KVRVELLNHP AFCSLATTKR
RHGGTUTIRP KSSLSEVYVI VLEK TQLQEV EYKAAVYHHT IDDVVRKSLK VVPEQIRMNK TVAVETLDFE RLDRGQVGR E
DIPFADLSDQ VPDTSETRI LLOGTTPVAGM TEDAVDAERL KHLIVTPOC GEONMIQMT P TVIAVHYLDE TEWEKFGLE
KRDGAELELK KGYTQQLAFR QRSAPAFV KRAPSTWLT A QVHSLFOSIT KADDFLEANT NLLQREBYVA IAGYALAQMG
DAPYHQREH OGLRNNERD MALTAPVLLS GSEAKDFICE VVHSLFOSIT KADDFLEANT NLLQREBYVA IAGYALAQMG
RLKGPLLNRF LTTAKDKNRW EDPGKGLYV EATSYALLAL LQKDFDFVP PVVRWLNQOR YVGGQYGSTO ATFMVFGALA
QYQKADPHQ ELLLDVSLQL PRRSKITH IHWESASLLR SEETENEGF TVTAEQGGD TLSVVTMYHA KAKDQLTCHK
FDLKYTIKRA LETEKRQDA KNTMILIEICT RYRQDQATM SILDISMHT PAPDIDLKQ LANGVDFEYR EYLDKAFSD
RNTLIIYLDK VSHSEDDCLA FKVHQYFVNE LIOPGAVKVV AYNLEESCT RFFVHPEKED KLNKLSPEEL GRCAEENCFI
QKSDDKVLE ERLDKACEFG VDVYKTRLV KVOLSNDFDE YIMAIETIK SSSDEWVQQ QRTTSPKIC REALKLEEKK
HYLMWGLSSD FWGKPNLSY IIGKDTWVEH WPEDECODE ENQKCCDLG AFTESMVVFG CPN
    
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C5

C05_HUMAN (100%), 188,309.2 Da
Complement C5
9 unique peptides, 9 unique spectra, 16 total spectra, 108,1676 amino acids (6% coverage)

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MGLLGLLCLF IFLDKTWQDE QTYVIBAPKI FRVGAASNIV IQVYGYTEFP DRTSISIKSYP DKNFSYSSQH VHLSENKFO
NSALTIQPK QLPQQQPVLS YVYVLEVSKH PSKKSPFIT BNGFLFPEP DAVVYTPDQS VKVRVYSLND DLKPAKRETV
LTFIDEGESE VDMVEIDHI GIIISFPDFKI ANRPRQWMT IAKYKEDDT TGTAYFEVK EYVLPHFVS IEPYENFIQY
KNFKNFPEITI KAMVFPYKVV TEADVYITFG IREDDQDOK EMMQTAMQIT MLINGIAQVT FDSATAVKEL SYSLSEDLNN
KYLIIAVTVI ESTQDFSEA EIPQIKYVLS PUNLAKTTP LLDKPGQVFP IKVQVKSLO QLVGGVFPVTL NADITDYNQE
TSLOLPSKSV VLNLPQGVTV LKRNKADAP DLSEKRE GYRAIAYSSL SGSVLYIDWT DNKALLVGE
HLNIIYTPKS PYIDKITHYN YLLLSKQKI HMOINRSD ASGSPNIPV TORMVPSRRL LVVYVLTQEQ TAEVSDSVW
LNIIEKCGHG LQVLSRDAD AYSPQOTVSL NMGNMDEG VLSKVDPAVY QVQEGAKKPL QVQEGAKKPL
NNANVFHLAQ LTFLTNANAD DSGNDEPCK ELLPRTTLO STIEEIAAKY KHSVVKCCCV DQACVNMDET GEORAAIRSL
GPRCIRAFTE CQVVASQLRA NISHLDMQLG RLH TLLFP SKPEIRSFVP ESWLWVHLV PRKQLGFAL PDLTTEIJD
GQGISNTGIC VADTVKAVYF KDVELEMNIF VYVLEAGDIO LKGTVYNTR SGMICVHMS AEGDGLSEES VVHQOQTS
SKCVRQKVEF SSSHLVFTV LPLEIOLHNI NPSLWTFQK EILVKTLRVY PEGVKKREYS GVTLDPRQIY QTISRRKEFP
YRIFLLVPK TEIKRILSVK GLLVQETLEA NLSGQINIL TMLPRKASACA ELMVYVAFH FPHALGTQNH WAFPHQDPLI
EKQKLLKXK EMGLSIMSRY NADYSYSVWK GGSASTWLT A FALRVLQGVN KYVEONONSI CNLSLWLVEN YOLDNGSFE
NSQYQPIKLG GTLVPEAREN SLYLTAFTVI QIRKAFDQCP LVHIDTALIK ADNFLLENTL PADSTFTLAI SAYALSQDR
THQFRSIVS ALKREALVKG NRPYRFFWKD NLOKHOSSVP NTQIARMVET TAYALLTSLH LNDIYNVNRV IOKWSEGRY
GGGFYSTQD INAIIEGLTEY SLLVKQLRLS MDIDVYRHKK GALHNKMTD KNFLGRPVEV LLNDDLIVST GFGSLATVH
DITVYHKTST DEEVCSPYLK IDTQDIASH YRQVGNSDYK RIVACASYKP SRESSSSSS HAVMDISLPT QISANEEDLK
NLYGQDQIF TDQYIKDGHV ILQLNSIPSS DFLCYRPRIF ELFEVQFLSP ATFTETEVEY DKKQCTMFYS TSNIKIKQVQ
EGAACKCIEA GCGMQEELD LTI SAETRQK TACKPEIAYA YKVSITSITV ENVFVKYKAT LLDIYKTGEA VAEKDSIIF
IKKVTCTNAE LVKRGQYLIM GKREALQIKYN FSFRYIYPLD SLTWIEYWRP DTTCSGQAF LANLDEFAED IFLNGC
    
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C9

C09_HUMAN (100%), 63,174.9 Da
Complement component C9
10 unique peptides, 13 unique spectra, 21 total spectra, 121,959 amino acids (22% coverage)

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MSACRSFAYA ICILEISILT AQYTTSDPE LTESSSGSASH IDCRMSPWSE WSQCDCPCLRO MFRSRSEIEVF GQFNKRCCTD
AVQDRQCCVP IEPCEDAEDD CQNDFOCSIG RCIKMRLRQN GQNDCCDFSD EDDCESEPRP PCRDRVVEES ELARTAGYGI
NLYGQDQIF TDQYIKDGHV ILQLNSIPSS DFLCYRPRIF ELFEVQFLSP ATFTETEVEY DKKQCTMFYS TSNIKIKQVQ
LKFTPTETHK AEQCCETAS SISLHGKGRF RFSYSKNETY QLFVLSYSSK EKMLVHKGE INLGRFVMR RDVVLTTTFV
DDIKALPTTY EKGDFAFLE TYDTHYSSSG SLOGLYELIY VLDKASMRPK QVELDINRC LGYHLDVSLA FSEISVGAEL
NDDCKVROE DRAYVYRGL LIDDVYSIR GQTRKAFEL KEHLHQTWV DVDFVHW E SINDARVLIS QKLSPIWNL
FVKMKNHLK KQNLERATED YINEFSVKKC HTCQGGTVI LMDGKCLAC PFKFEGIAE ISKGRISEGL PALEFPNEK
    
```



What is the relationship of post-infectious GN to C3 glomerulopathy: two different or related entities

- Clinical presentation/duration of kidney disease
- Pattern- diffuse proliferative GN
- Presence of IgG + C3 versus C3 only
- Subepithelial humps
- Ancillary studies- C4d

Atypical postinfectious glomerulonephritis is associated with abnormalities in the alternative pathway of complement

Sanjeev Sethi¹, Fernando C. Fervenza², Yuzhou Zhang³, Ladan Zand², Nicole C. Meyer³, Nicolò Borsa³, Samih H. Nasr¹ and Richard J.H. Smith^{3,4,5}

Electron Microscopy

- Required in every case?
- Overlapping features

KDIGO