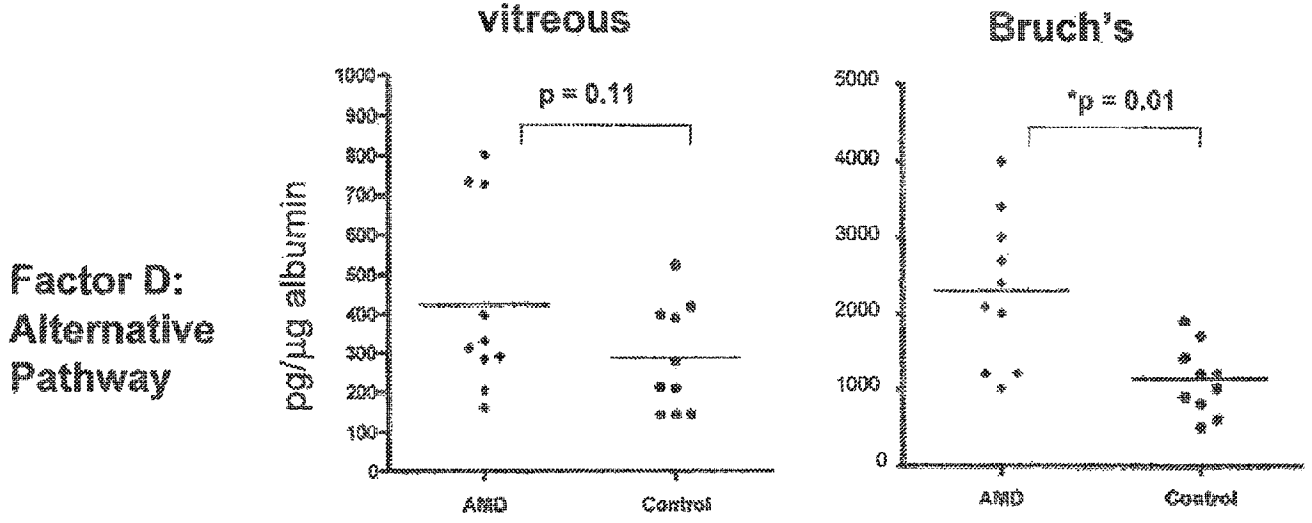
Increased factor D expression in Bruch's membrane of AMD eyes

A



B

	Plasma	AMD (*tot eye*) (Bruchs+vitreous)	Control (*tot eye*) (Bruchs+vitreous)
fD (nM)	42	15 *(6-32)*	11 *(4-24)*
plasma eq. (%)	100	36	26

Figure 1

Factor D is present in druse, Bruch's and choroid in an AMD donor

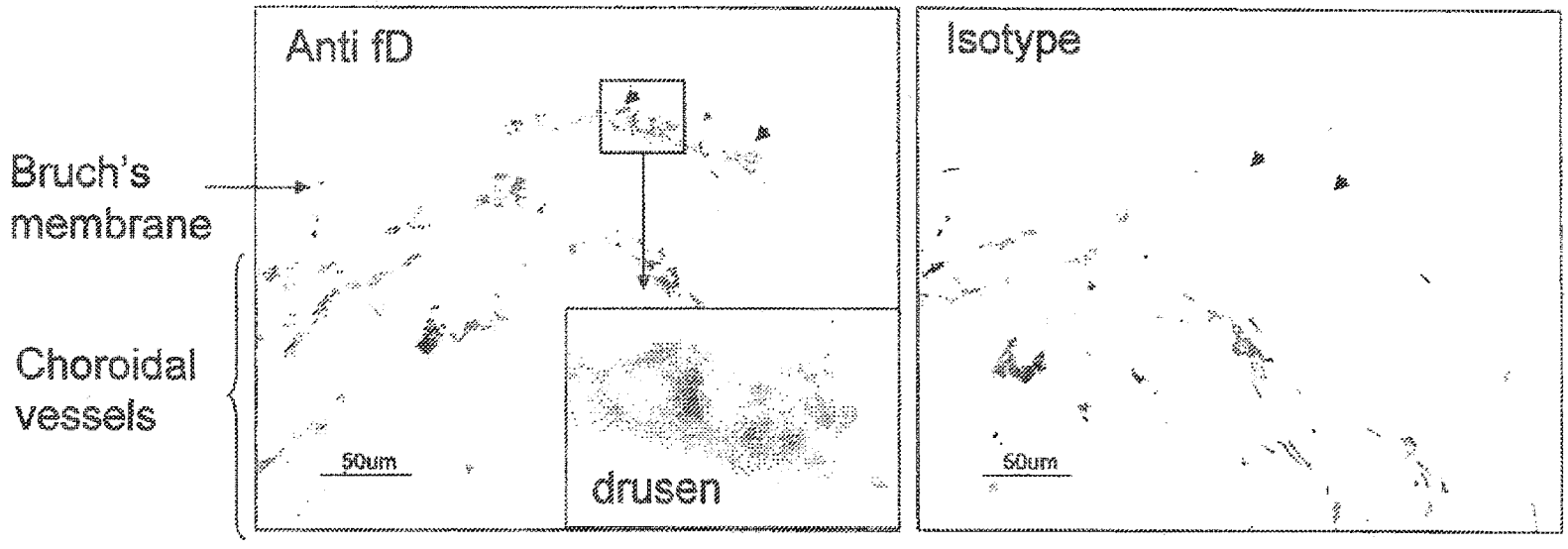
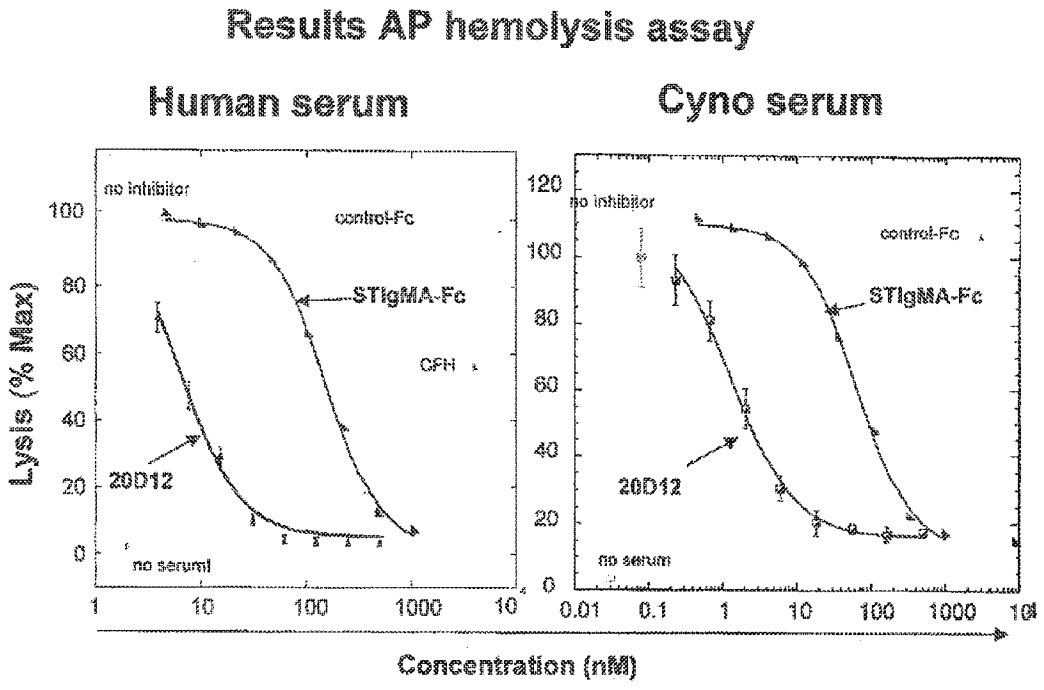


Figure 2

Characterization of factor D antibody clone 20D12



	epitope	IC50 (nM)	Ratio*	IC90 (nM)
20D12	B	1.3	0.02	9.3

* Ratio IC50 αfD/STIgMA-Fc

Figure 3

Sequence of antibody 20D12

Light chain sequence 20D12:

MGWSCIILFLVATATGVHSDIVMTQSQKFMSTSVGDRVSVTCKASQNVDTD
VAWFQQKPGQSPRGLIYSASSRYSGVPDRFTGSGSGTDFTLTISNVQSEDL
AEYFCQQYNNYPLTFGSGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCL
LNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADY
EKHKVYACEVTHQGLSSPVTKSFNRGEC

Heavy chain sequence 20D12

MGWSCIILFLVATATGAYAQVQLQQSGAELVKPGASVKLSCKASGYTFTSY
YMYWVKERPGQGLEWIGEINPTNGGTNFNEKFKSKATLTVDTSSNTAYMQ
LSSLTSEDSAVYYCAREGGFAYWGQGTLVTVSAASTKGPSVFPLAPSSKS
TSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS
VVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI
SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ
PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK

Figure 4

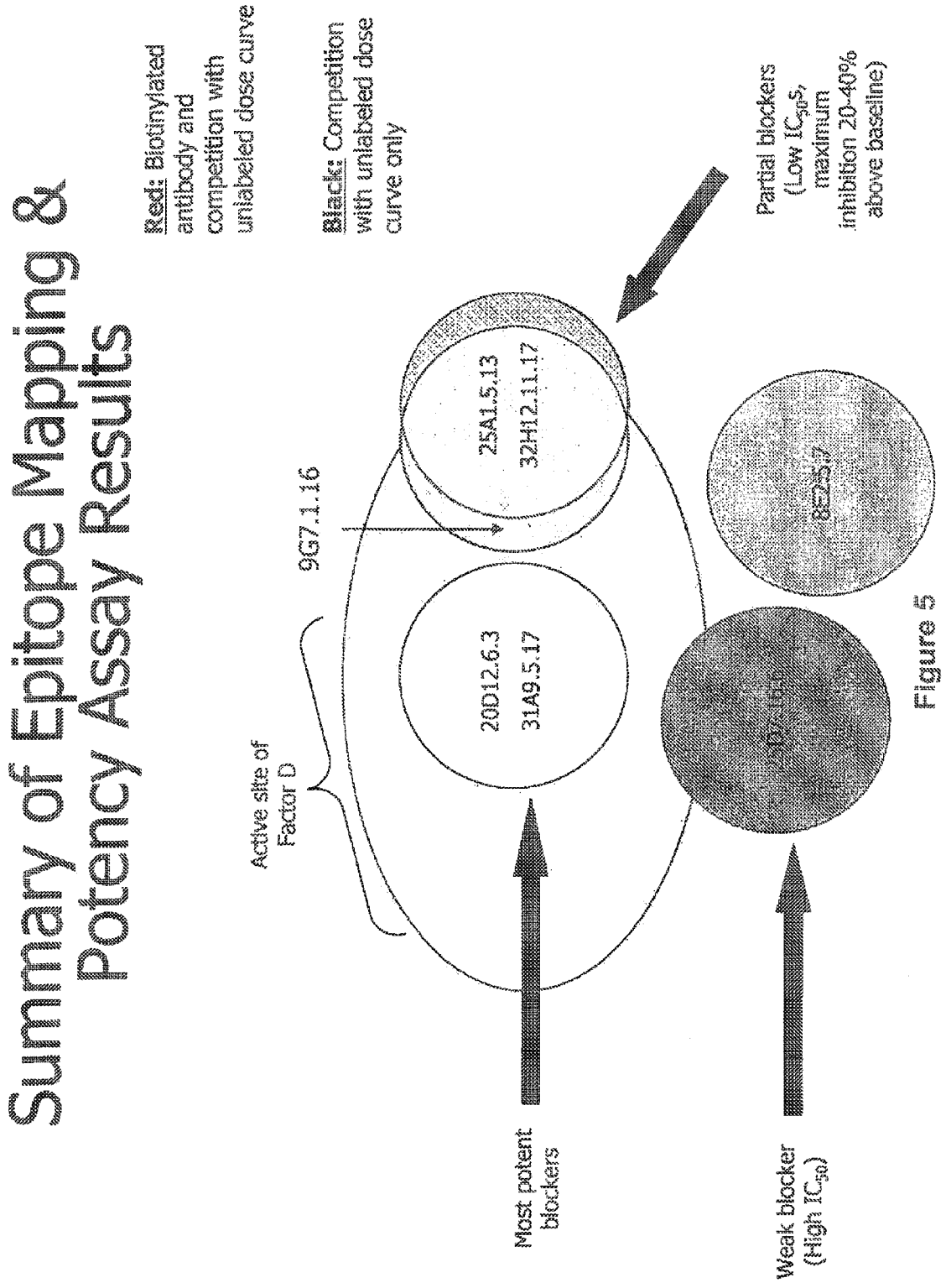

Summary of Epitope Mapping & Potency Assay Results
Red: Biotinylated antibody and competition with unlabeled dose curve
Black: Competition with unlabeled dose curve only
Active site of Factor D
9G7.1.16
20D12.6.3
31A9.5.17
25A1.5.13
32H12.11.17
Partial blockers (Low IC50s, maximum inhibition 20-40% above baseline)
Most potent blockers
Weak blocker (High IC50)

Figure 5

Figure 6

Human complement factor D (NP_038487.1)

1 MHSSVYFVAL VILGAAVCAA QPRGRILGGQ EAAAHARPYM
41 ASVQVNGTHV CGGTLLDEQW VLSAAHCMDG VTDDDSVQVL
81 LGAHSLSAPE PYKRWYDVQS VVPHPGSRPD SLEDDLILFK
121 LSQNASLGPH VRPLPLQYED KEVEPGTLCD VAGWGVVTHA
161 GRRPDVLHQL RVSIMNRTTC NLRTYHDGVV TINMMCAESN
201 RRDTCRGDSG SPLVCGDAVE GVVTWGSRVC GNGKKPGVYT
241 RVSSYRMWIE NITNGNMTS

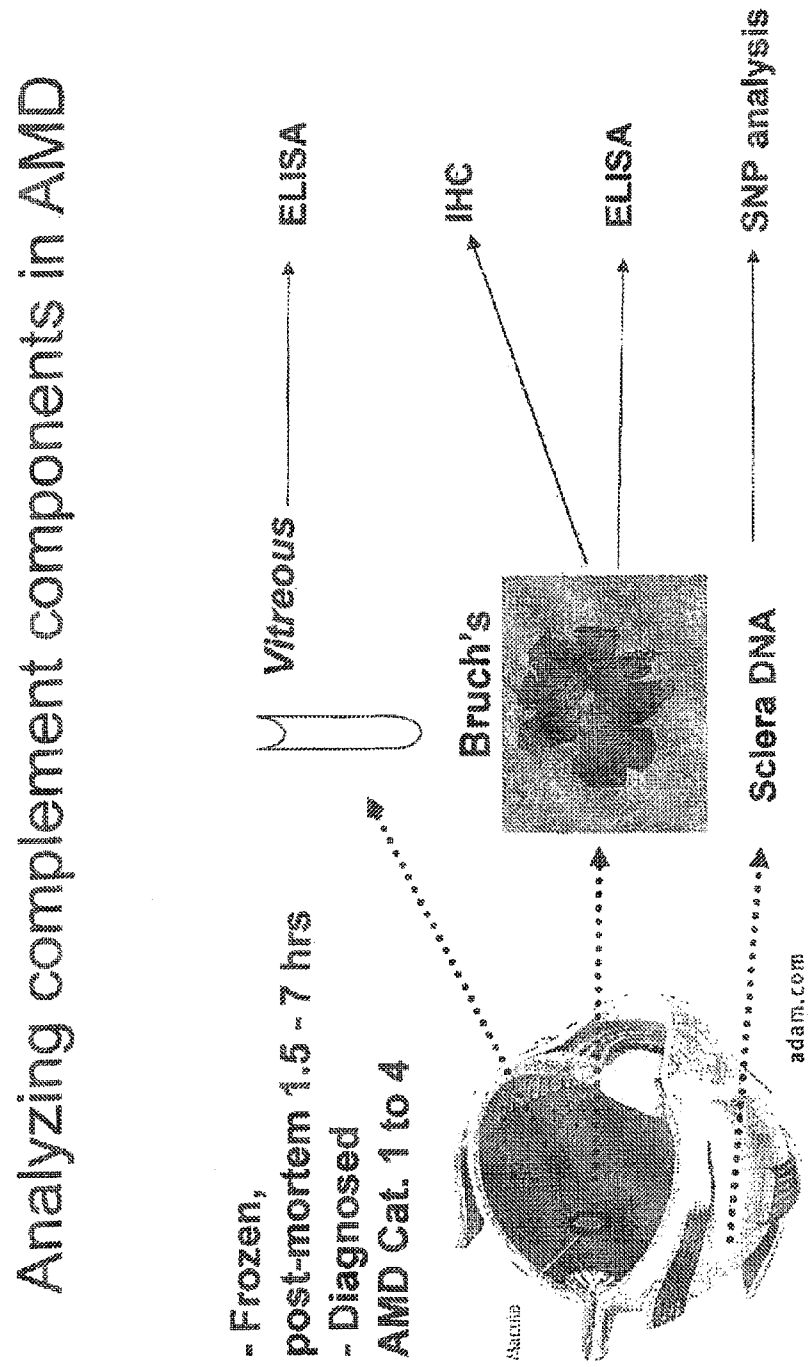

Analyzing complement components in AMD
- Frozen, post-mortem 1.5 - 7 hrs
- Diagnosed AMD Cat. 1 to 4
Vitreous
ELISA
IHC
Bruch's
ELISA
SNP analysis
Sclera DNA
adam.com

Figure 7

Donor tissues used in the studies

Genentech #	Age	Sex	AMD Stage	Disection notes
1	78	F	3	Foveal scar, few macular drusen **FS**
1A	78	F		No drusen evident
2	85	M	4	Geographic Atrophy **GA**
2A	85	F		No drusen evident
3	87	F	4	Fibrovascular scar in fovea **FS**
3A	87	F		No drusen evident
4	76	M	4	Geographic Atrophy **GA**
4A	74	M		Two small drusen present
5	81	F	3+	Moderate macular drusen **MD**
5A	81	M		No drusen evident
6	84	F	3	Numerous macular drusen **MD**
6A	86	M		No drusen evident
7	83	F	4	Fibrovascular scar in fovea **FS**
7A	83	M		No drusen evident
8	72	M	4	Foveal scar, Moderate macular drusen **FS**
8A	71	F		No drusen evident
9	81	F	4	Foveal scar, Moderate macular drusen **FS**
9A	83	M		No drusen evident
10	77	M	3	Numerous macular drusen **MD**
10A	78	M		No drusen evident

☐ Geographic atrophy
☐ Foveal scar
☐ Stage 3 AMD

Figure 8