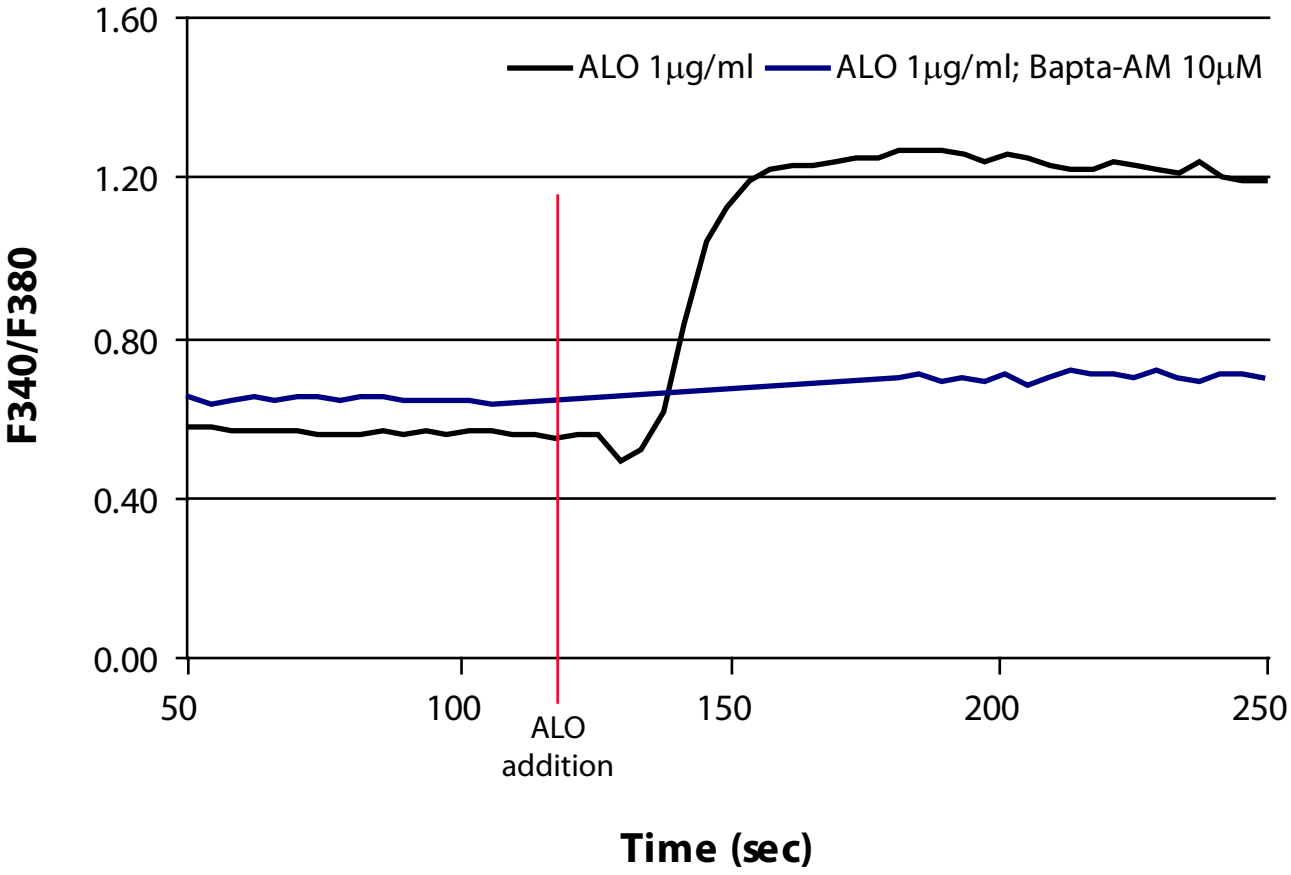
Supplementary Table 1. RMSD values (Å) from superposition of C-α atoms			
	PFO (I)	PFO (III)	ILY
ALO D1	1.841	1.803	1.479
ALO D2	2.105	2.634	3.1
ALO D3	2.064	2.183	2.915
ALO D4	2.76	2.013	2.201
ALO D1-D4	3.838	4.902	4.553

Supplementary Table 2. Hydrodynamic Parameters		
	From QELS & TDA	From PDB
Ro (nm)	2.5	2.5
RH (nm)	2.9 ± 0.1	3.5 ± 0.1
Frictional ratio (f/fo)	1.16 ± 0.04	1.4 ± 0.1
Molecular mass (kg/mol)	53.6 ± 0.4	54.0
Intrinsic viscosity (ml/g)	5.1 ± 0.2	5.5 ± 0.2
Hydration (g/g)	0.4 ± 0.1	0.2 ± 0.03
Viscosity increment	4.5 ± 0.6	6 ± 0.4
a/b	3.8 ± 0.4	5.2 ± 0.3
a (nm)	7.1 ± 0.4	9 ± 0.9
b (nm)	1.9 ± 0.05	1.7 ± 0.2

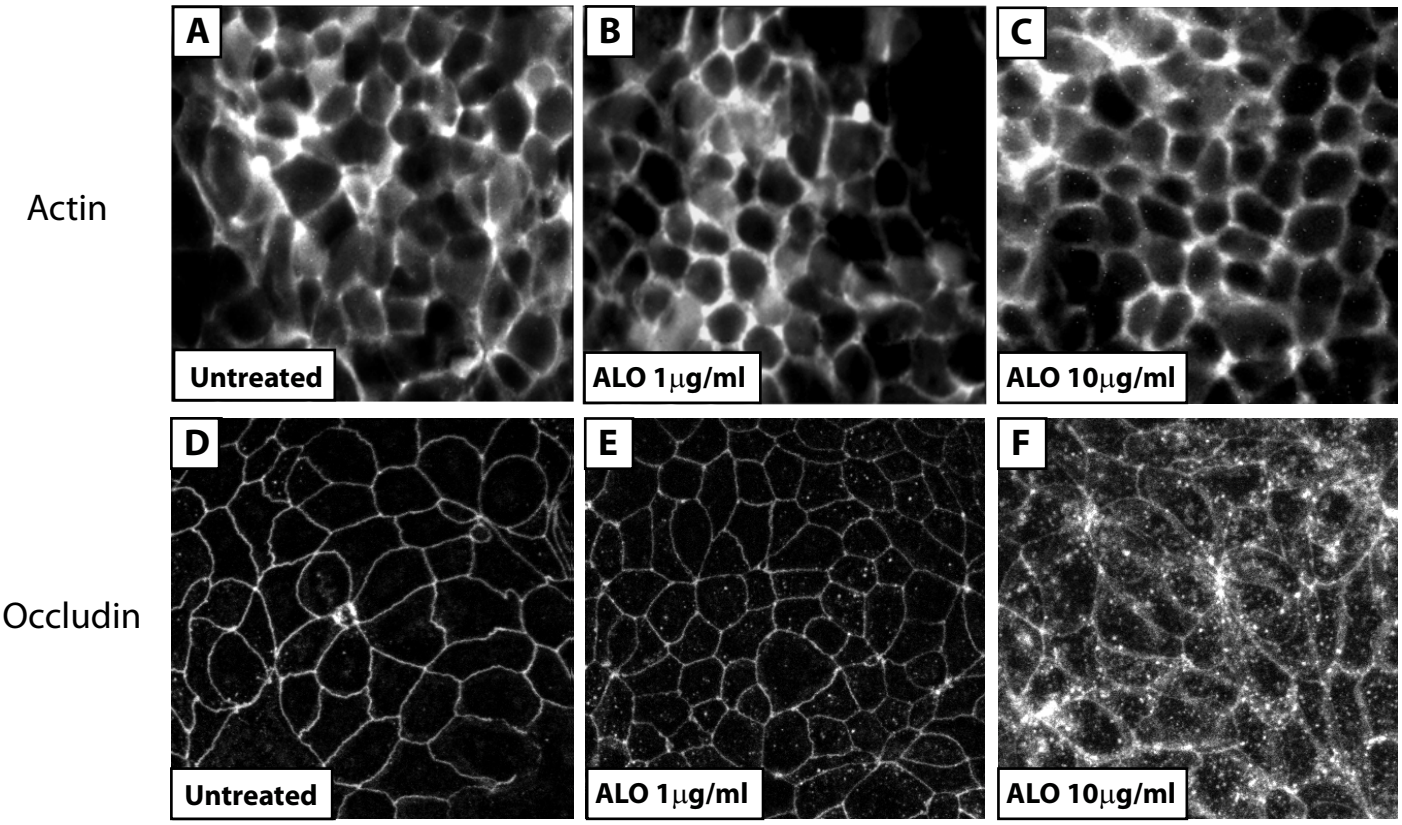
Supplementary Table 3. Sedimentation Velocity statistics			
	H6-ALO	H6-ALO	H6-ALO
Data Collection			
Instrument	Beckman Optima XLA	Beckman Optima XLA	Beckman Optima XLA
Buffer	20 mM Sodium Citrate + 100 mM NaCl	20 mM HEPES + 100 mM NaCl	20 mM Tris + 100 mM NaCl
pH	5.5	7.0	8.0
Points collected	300	220	220
Refinement			
Points refined	100	100	100
Resolution	200	100	100
Meniscus (cm)	6.1043	6.0190	5.9415
Bottom (cm)	7.2275	7.2419	7.2253
Friction ratio	1.568001	1.395	1.365
Rmsd	0.009248	0.013181	0.013379
c(M) analysis			
Monomer	0.907440 (91.67%)	0.772204 (97.505%)	0.834108 (97.78%)
Avg MW (Dal)	53413	53872	53847
Dimer	.051029 (5.127%)	---	---
Avg MW (Dal)	107201	---	---
Trimer	.016593 (1.6675)	---	---
Avg MW (Dal)	157720	---	---

Supplemental Figure 1



BAPTA-AM treatement of C2BBE monolayers reduces ALO-induced calcium flux. C2BBE monolayers were treated with the calcium chelator BAPTA-AM (10μM) for 45min prior to calcium flux imaging as detailed in the materials and methods. The Fura2 fluorometric ratio of 340nm/380nm was recorded over time to quantify the amount of intracellular calcium both prior to (left of red line) and after (right of red line) ALO treatment (1μg/ml) of C2BBE monolayers. Control C2BBE monolayer treatment with ALO induced a calcium flux within seconds after treatment (blackline). Calcium flux within BAPTA-AM treated C2BBE monolayers was not seen after ALO treatment (blue line). This figure is the average of 20-25 individual cells.

Supplemental Figure 2



Supplemental Figure 2 - Cytoskeletal localization of actin does not change during ALO treatment. C2BBE monolayers are either left untreated (A,D), treated with ALO at 1µg/ml (B,E) or ALO at 10µg/ml (C,F) for 2hrs. Monolayers labeled with Alexa Fluor 680 phalloidin (A-C), which labels polymerized actin, shows little ALO dependent rearrangement. For comparison, the same C2BBE monolayers labeled with anti-occludin antibodies from Fig. 2 are included. In addition, C2BBE monolayers treated with ALO (1µg/ml) shows an intermediate phenotype, as occludin is mostly located at the cell periphery but intracellular puncate staining is detectable.