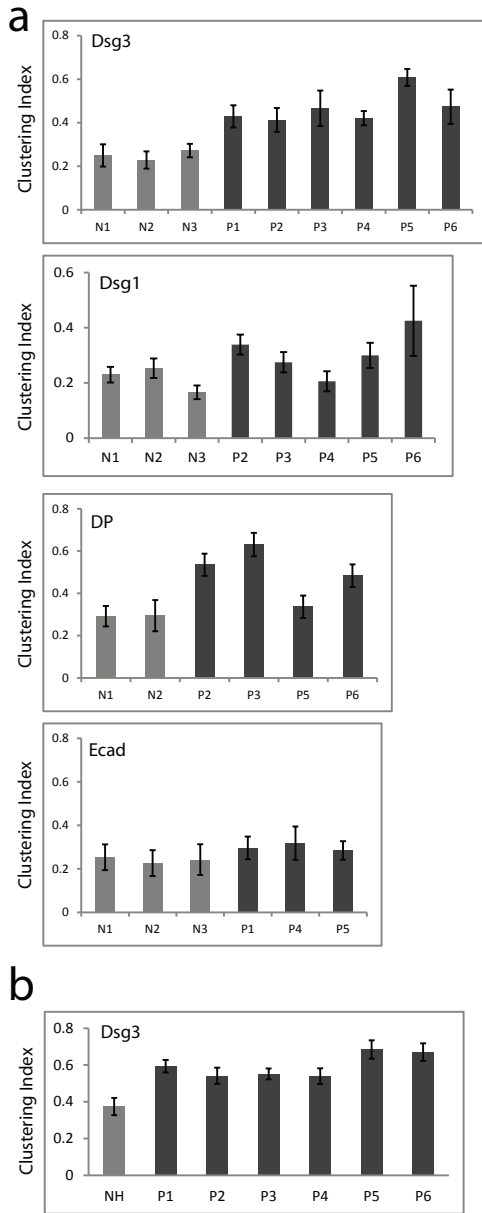
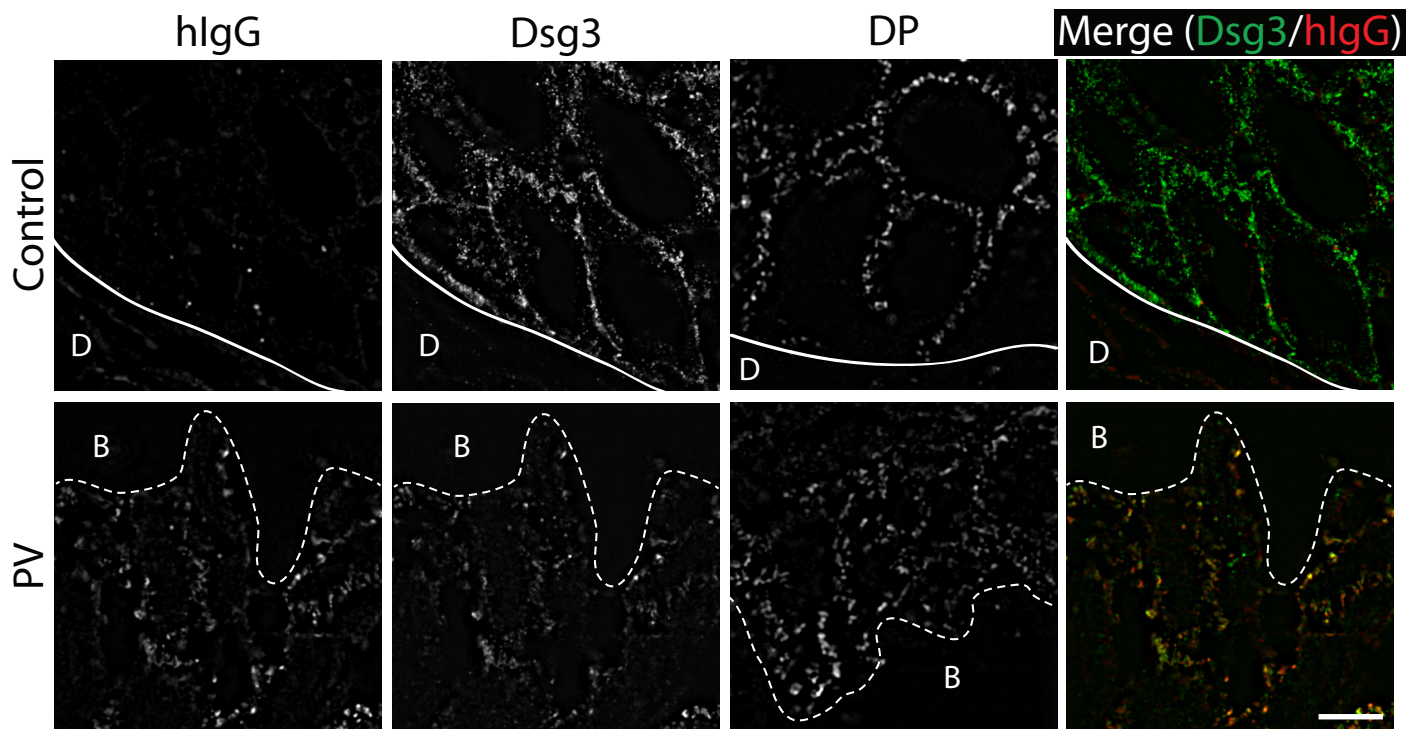


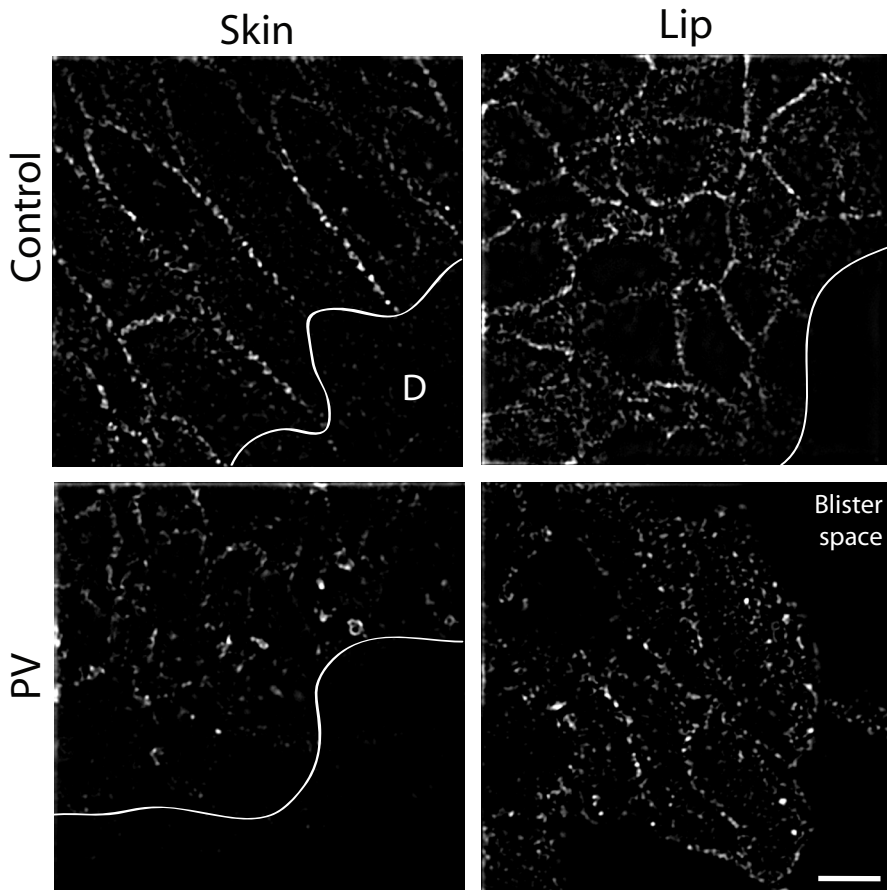
Supplemental Figure 1. Comparison of widefield to super-resolution microscopy. (a) Representative images of control and PV epidermis stained for Dsg3 (AK15) and imaged by either widefield (WF) microscopy at 63x or structured illumination microscopy (SIM) at 100x to show the SIM field of view in Figures 1-3 and Figures S3-S4. (b) Direct comparison at 100x of patient tissue stained for desmoplakin (DP) and hIgG imaged by widefield and SIM. D, dermis. Solid line, dermis interface. B, blister space. Images oriented dermis down. Scale bar, 10 μm (a) and 5 μm (b).



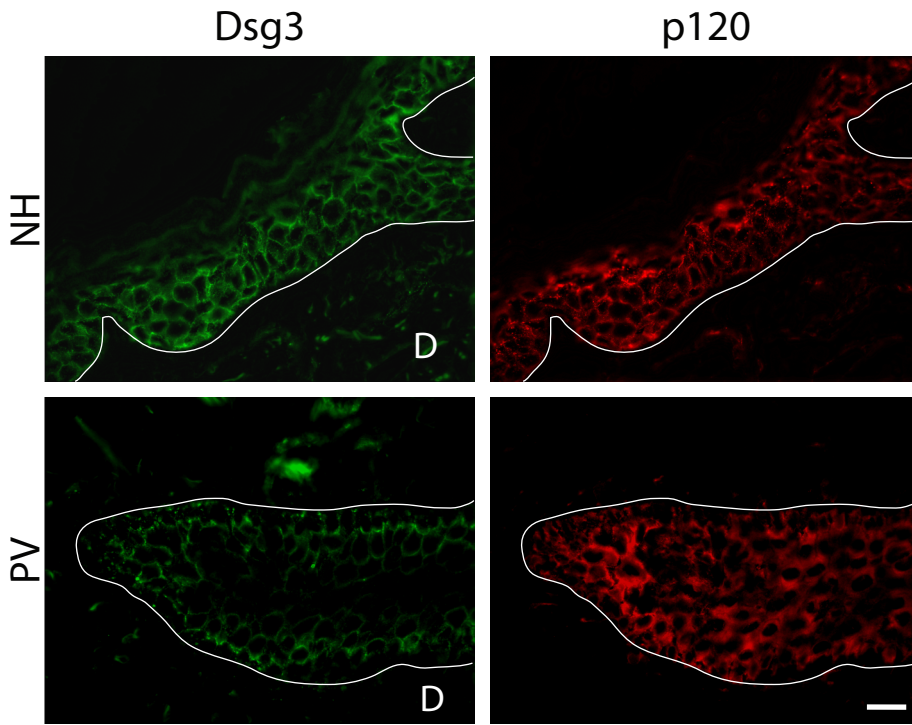
Supplemental Figure 2. Clustering analysis of individual patient samples used in Figure 1. (a) Quantification of Dsg3, Dsg1, desmoplakin (DP) and E-cadherin (Ecad) clustering. **(b)** Quantification of Dsg3 clustering in cultured keratinocytes exposed to either NH IgG or IgG from PV patients (P) 1-6.



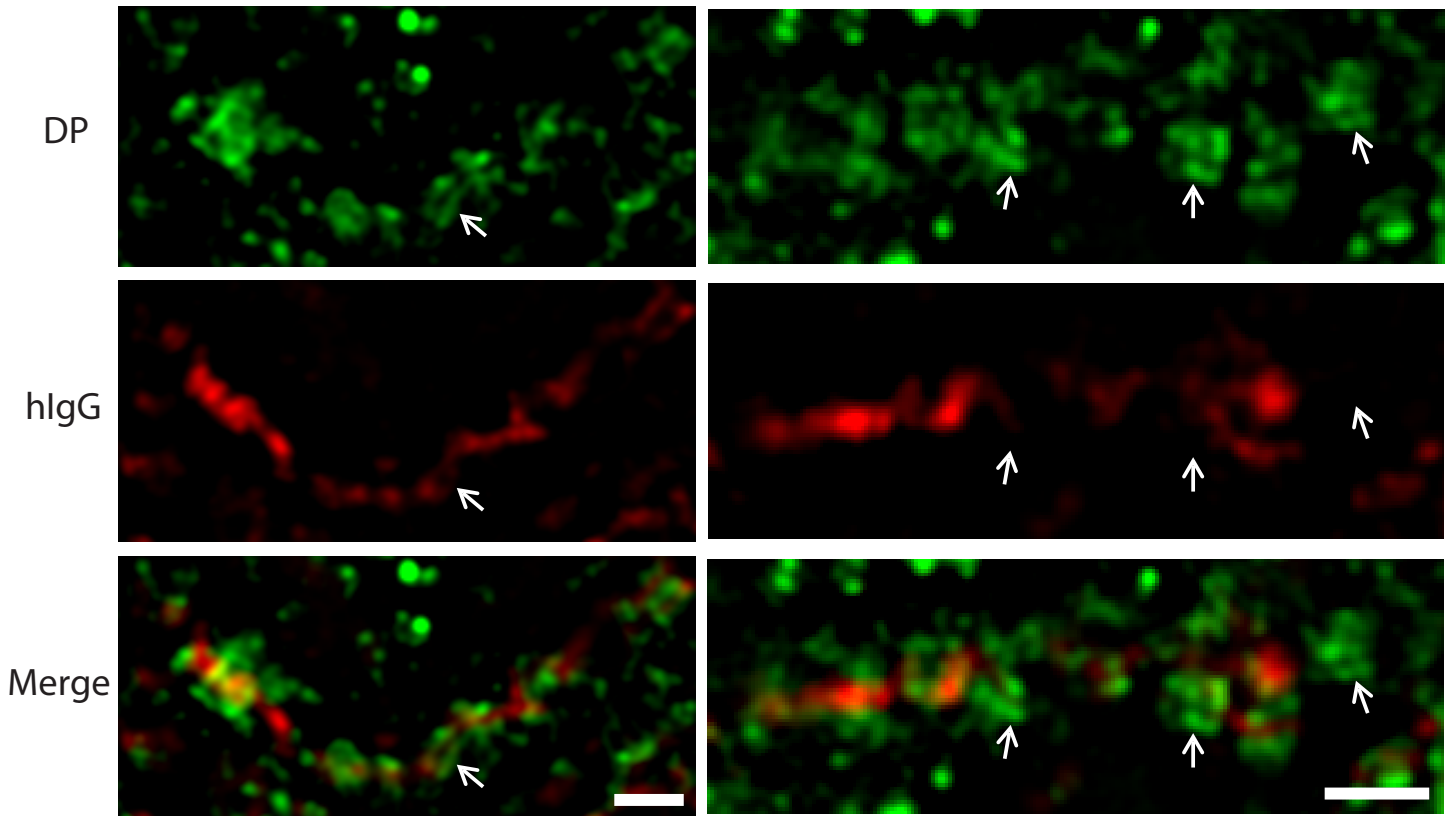
Supplemental Figure 3. Altered desmosomal protein organization in PV patient lip tissue. Top panel: Tissue from a patient with mucous membrane pemphigoid, which targets hemidesmosomes but not desmosomes, was used as a non-PV control for the lip biopsy site (patient's Dsg ELISA and direct IF were negative). This control (non-PV) mucosal tissue is negative for IgG (hIgG) deposition and junctional proteins desmoglein 3 (Dsg3) and desmoplakin (DP) uniformly distributed along cell borders. Bottom panel: PV patient mucosa is positive for hIgG deposition and border localization of Dsg3 and DP is highly disorganized and clustered. D, dermis. Solid line, dermis interface. B, blister space. Dashed line, blister floor or roof. Images oriented dermis down. Images from P5-6. Scale bar, 5 μ m.



Supplemental Figure 4. Altered plakoglobin organization in PV patient tissue. Top panel: Control (NH, skin and non-PV, lip) tissue displays uniform border localization of plakoglobin. Bottom panel: Disrupted and clustered plakoglobin staining in PV patient tissue. D, dermis. Solid line, dermis interface. B, blister space. Images are oriented dermis down. Images from P2, 5. Scale bar, 5 μm .



Supplemental Figure 5. Dsg3 levels are decreased in PV patient tissue. Dsg3 levels were analyzed by wide-field microscopy and normalized to adherens junction protein p120 (Figure 3b). Total Dsg3 levels were decreased in PV patient tissue, particularly in basal cell keratinocytes. D, dermis. Solid line, epidermis-dermis interface. Images from P2. Scale bar, 20 μ m.



Supplemental Figure 6. Dsg-depleted desmosomes in PV patient tissue. Patient tissue stained for desmoplakin (DP, green) and hIgG (red). Images cropped to highlight horizontal cell-cell borders. Arrows highlight desmosome railroad tracks lacking hIgG staining. Images from P1. Scale bar, 1 μm .

Patient ID*	Age	Gender	Disease Duration	Treatment**	ELISA Score		PDAI	Biopsy Site
					α -Dsg1	α -Dsg3		
P1	45	male	2 months	prednisone 40mg, imuran 150mg	128	178	23	skin
P2	51	female	10 years (3 mos current flare)	topical steroid	217	146	53	
P3	31	female	11 months	prednisone 80mg, dapsone 125mg	18	166	14.6	
P4	63	male	8 months	prednisone 60mg	176	196	26.3	lip
P5	38	male	4 months	prednisone 30mg	36	164	55	
P6	54	female	6 months	none	0	114	17	

* all patients clinically classified as mucocutaneous

** at time of biopsy

Supplemental Table 1. PV patient characteristics.