Supplementary Online Content

Uribe P, Collgros H, Scolyer RA, Menzies SW, Guitera P. In vivo reflectance confocal microscopy for the diagnosis of melanoma and melanotic macules of the lip. *JAMA Dermatol*. Published online May 3, 2017. doi:10.1001/jamadermatol.2017.0504

This supplementary material has been provided by the authors to give readers additional information about their work.

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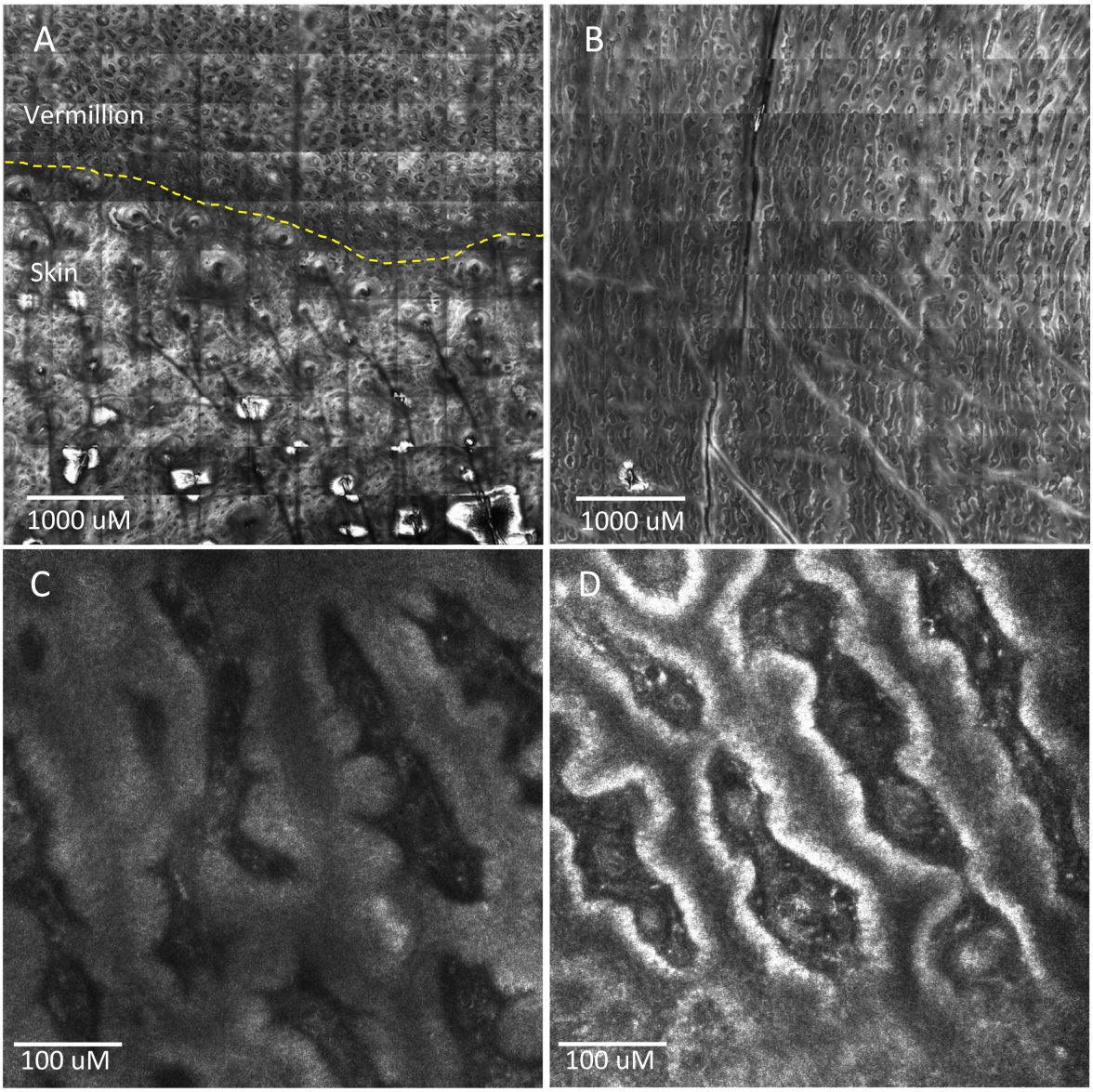
eTable 1. Dermoscopic findings in melanotic macules and melanomas of the lip

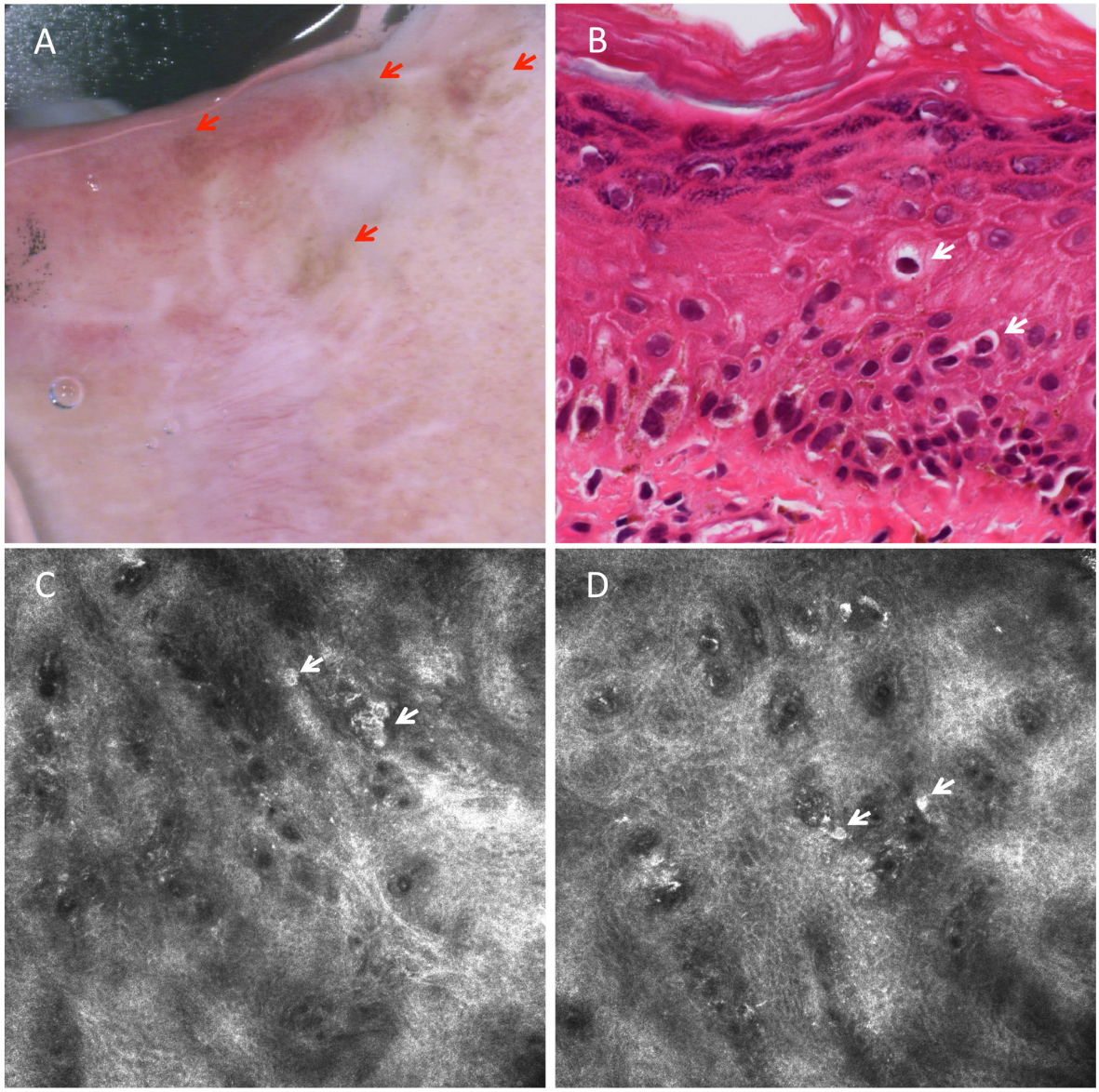
	Melanotic macules		Melanomas		*P*-Value
Dermoscopic pattern					
Structureless	4/16 (25%)		5/6 (83%)		**0.0231**
Lines	10/16 (63%)		2/6 (33%)		0.3476
Parallel	8/16 (50%)		2/6 (33%)		0.6462
Reticular	1/16 (6%)		2/6 (33%)		0.1688
Curved	6/16 (38%)		2/6 (33%)		1
Circles	3/16 (19%)		2/6 (33%)		0.5853
Globules/clods	9/16 (56%)		5/6 (83%)		0.3512
Dots	6/16 (38%)		3/6 (50%)		0.6550
Number of patterns					0.1982
1	6/16 (38%)		1/6 (17%)		0.6158
2	5/16 (31%)		1/6 (17%)		0.6341
3	5/16 (31%)		2/6 (33%)		1
4	0/16 (0%)		2/6 (33%)		0.0649
Predominant Pattern					
Structureless	1/16 (6%)		3/6 (50%)		**0.0458**
Lines	6/16 (38%)		1/6 (17%)		0.6158
Circles	1/16 (6%)		0/6 (0%)		1
Globules/clods	5/16 (31%)		1/6 (17%)		0.6341
Dots	3/16 (19%)		1/6 (17%)		1
Colour					
Brown	12/16 (75%)		5/6 (83%)		1
Black	1/16 (6%)		1/6 (17%)		0.4805
Blue	3/16 (19%)		1/6 (17%)		1
Gray	13/16 (81%)		5/6 (83%)		1
Red	–		–		–
Purple	–		–		–
White	0/16 (0%)		1/6 (17%)		0.2727
Number of Colours					0.7045
1	6/16 (38%)		1/6 (17%)		0.6158
2	7/16 (43%)		3/6 (50%)		1
3	3/16 (19%)		2/6 (33%)		0.5853
4	–		–		–
Symmetry of pattern	5/16 (31%)		1/6 (17%)		0.6341
Final Diagnosis					
Benign	13/16 (81%)		1/6 (17%)		
Equivocal	3/16 (19%)		4/6 (67%)		
Malignant	0/16 (0%)		1/6 (17%)		

Online-only Figures

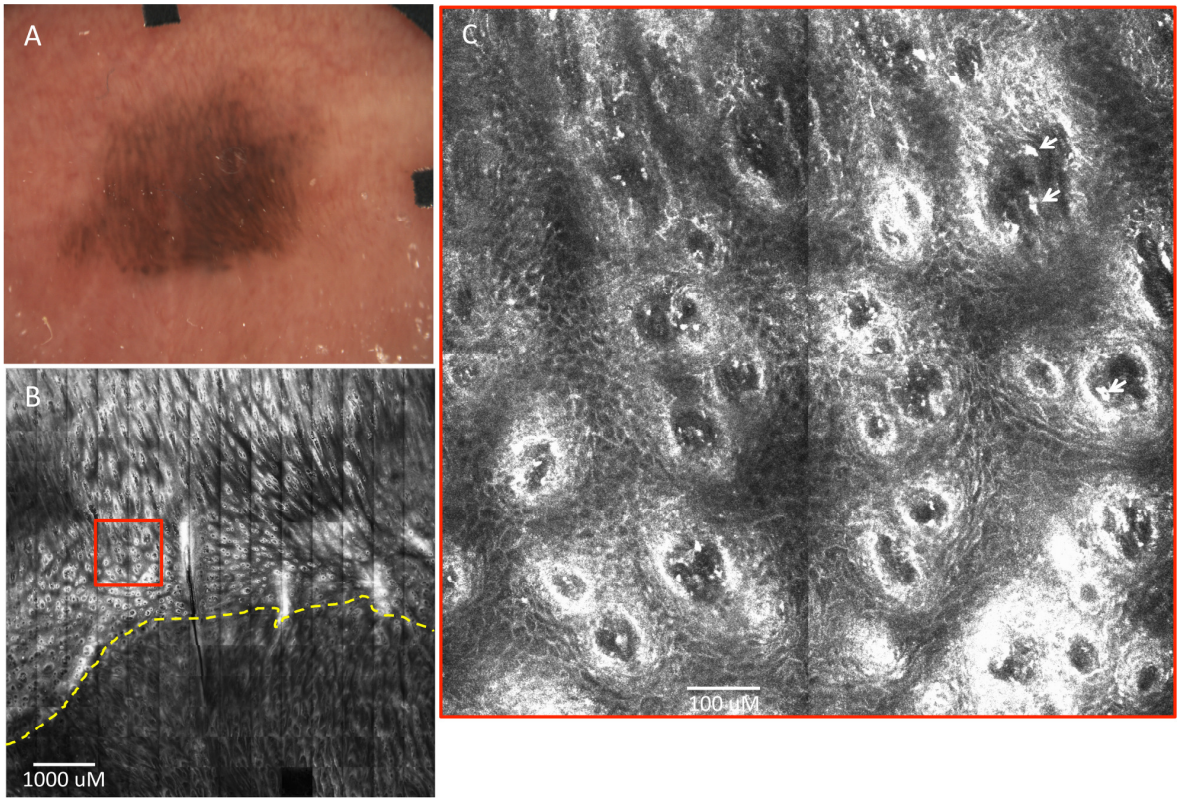
eFigure 1. *In vivo* confocal images from normal lower lip showing the draped pattern in two patients: (a,c), phototype II; B,D: phototype IV. (a), RCM at the junction level of the vermillion border. (b), RCM at the junction level of the vermillion area. (c-d), Draped pattern in the vermillion of patients with different phototypes.



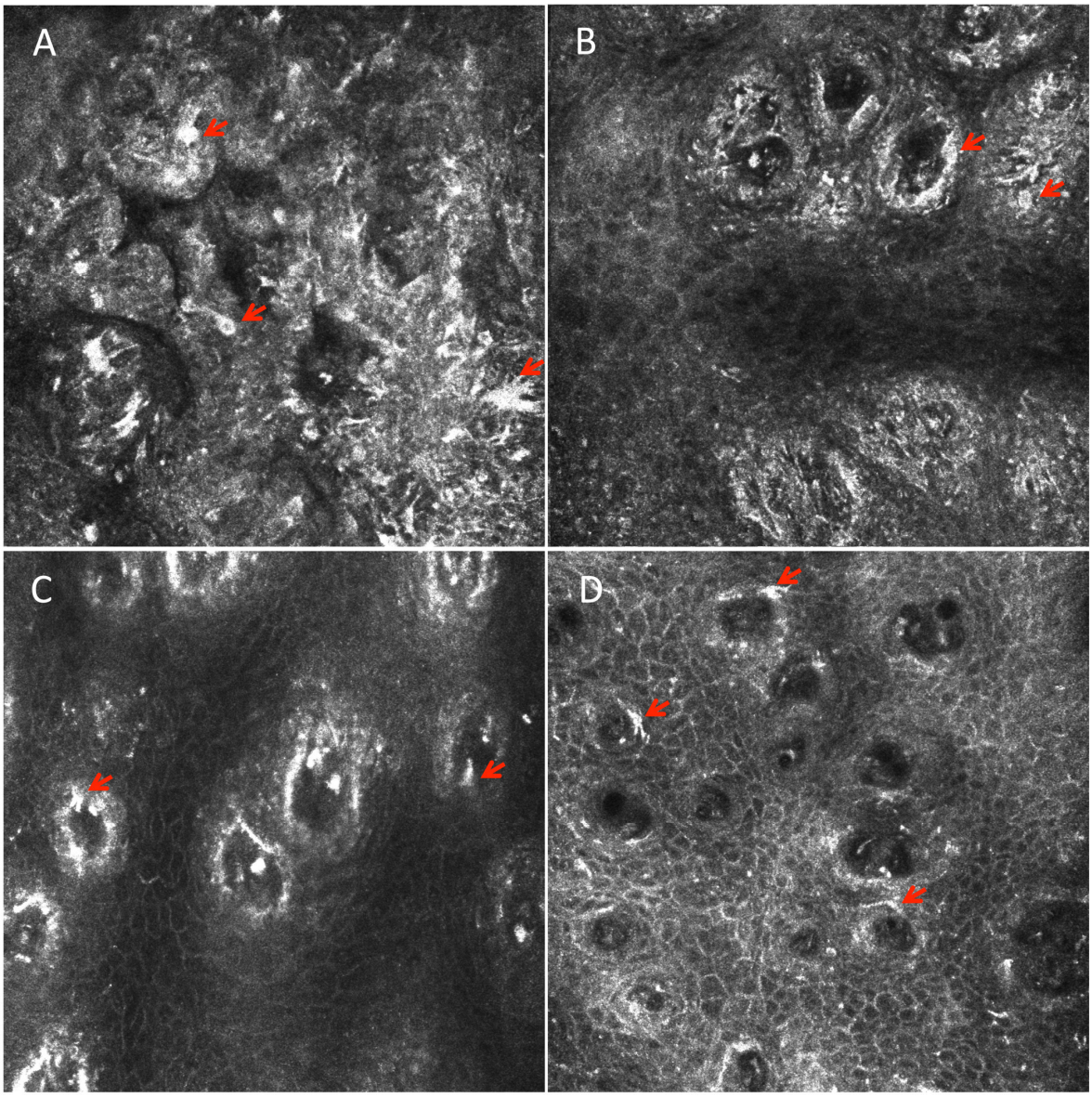
eFigure 2. Patient with a recurrent in situ melanoma on her lower lip. (a), Dermoscopy shows a white structureless area admixed with some brown and grey dots (red arrows). It was classified as equivocal by dermoscopy. (b), Histopathology demonstrated a lentiginous proliferation of atypical melanocytes and rare pagetoid cells (white arrows) consistent with lentigo maligna. (c-d), RCM shows non-homogeneously distributed papillae with isolated and nested dendritic pagetoid cells (white arrows).



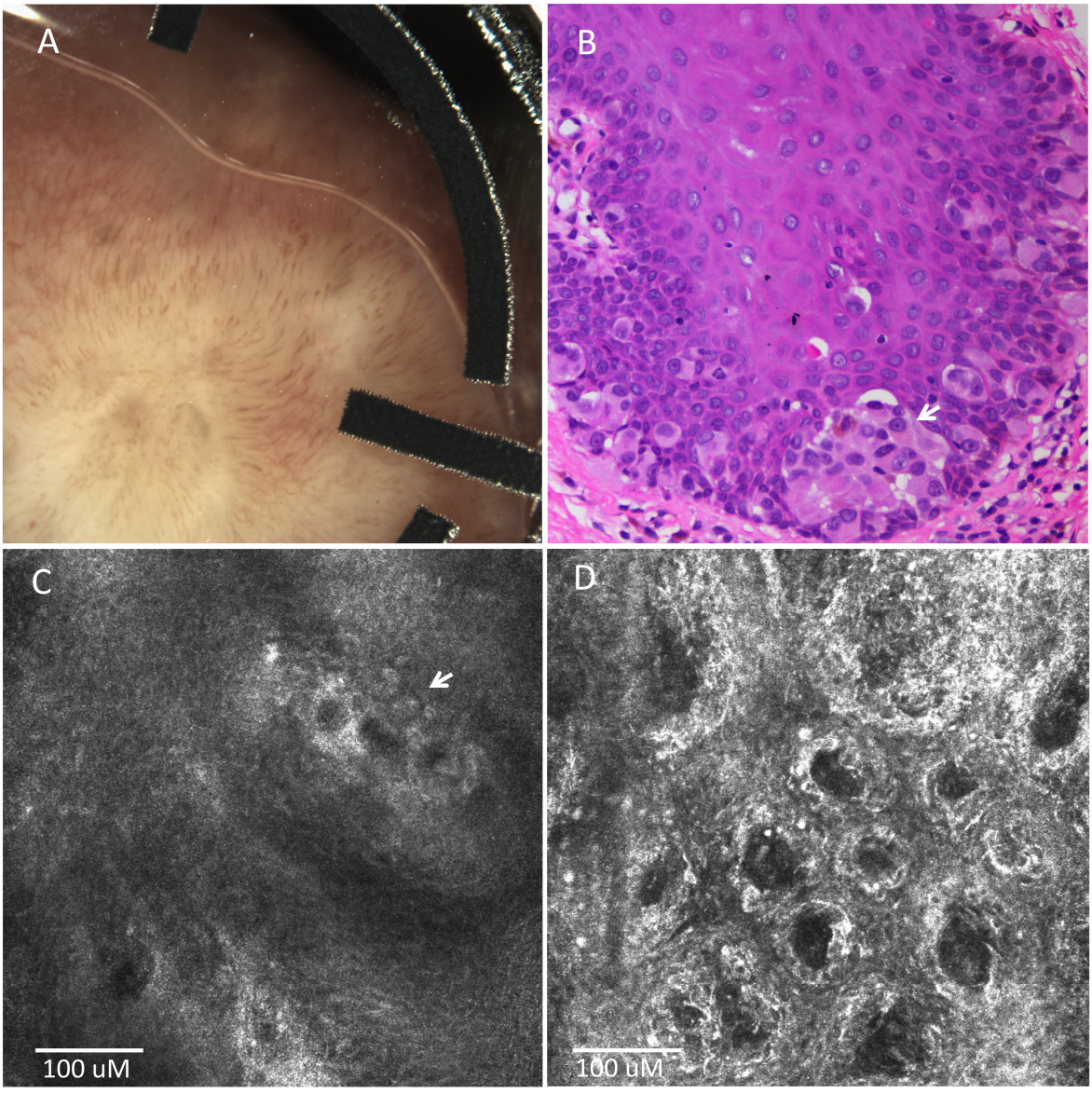
eFigure 3. Melanotic macule from the vermillion and part of the inner mucosae in a patient with an Asiatic background. (a), A predominant parallel pattern made of brown and grey lines is observed. (b), RCM mosaic (7 x 7 mm) at the DEJ: the normal draped or trabecular pattern is interrupted by a more reflective area which corresponds to the melanotic macule. The parallel pattern seen by dermoscopy is explained by the hyper-reflective papillae. (c), Selected area (1 x 1 mm) from the previous RCM mosaic (b). Homogeneously distributed nonedged papillae, characterized by the presence of sparse dendritic cells around the papillae. Some of the dendritic cells can be seen in the interpapillary spaces (red arrows) and others seem to be in the papillae (white arrows).



eFigure 4. RCM representative examples of differences in dendritic cells morphology between melanoma (a-b) and melanotic macules (c-d). In melanoma the body of the largest dendritic cells tends to be larger and rounder than in melanotic macules (red arrows shows some dendritic cells).



eFigure5 . Patients with lip melanomas. (a), Patient with a previous superficial spreading melanoma of the upper lip, with a recurrent *in situ* melanoma. While the dermoscopy image on the inner lip shows some scattered grey globules/clods, the pattern is nearly symmetrical. It was classified as benign by a blinded researcher. (b), Histopathology (H-E, 40X) shows very large and pleomorphic atypical melanocytes as isolated basal single cells and forming occasional nests (white arrow), with some pagetoid spread. (c), RCM at the DEJ: nest of large round cells (white arrow). (d), Patient with an upper lip melanoma. RCM at DEJ shows nonedged papillae with continuous (lentiginous) proliferation of atypical enlarged bright dendritic cells with some atypical cells in the interpapillary spaces (rete ridges), which correlates with histology (data not shown).



eFigure 6. Patient with a changing lower lip pigmented macule. (a), Dermoscopy shows a macule consisting of brown and grey curved lines, structureless brown areas and grey dots. It was interpreted as benign. (b), The histopathology shows basal pigmented keratinocytes, occasional junctional melanocytes and melanophages in the superficial dermis, interpreted as a melanotic macule. Also some brown lines that could correspond to pigmented dendritic processes. (c-g), selected RCM Vivastack images at different depth. (c), some small pagetoid cells and dendritic processes (bright filaments) in upper levels. (d), mainly dendritic processes and some dendritic cells in mid levels. (e), RCM at DEJ level reveals basal pigmented keratinocytes admixed with some small dendritic cells and dendritic processes. (f-g), RCM in the papillary dermis shows multiple plump bright cells in large aggregation and small bright particles.