

## Supplementary Material

**Table S1.** IHC staining conditions for each core circadian protein analysed.

Protein	Conditions	
	Antigen Retrieval	Primary Antibody
CRY-1	CC1 <sup>a</sup> (pH 8.4, 24 min)	30 min, 37 °C
CRY-2	CC1 <sup>a</sup> (pH 8.4, 1 h)	32 min, 37 °C
PER-1	CC1 <sup>a</sup> (pH 8.4, 48 min)	1 h, 37 °C
PER-2	Ribo CC o CC2 <sup>b</sup> (pH 6, 24 min)	1 h, 37 °C
PER-3	Ribo CC o CC2 <sup>b</sup> (pH 6, 24 min)	1/50, 1 h, 37 °C
Bmal1	CC1 <sup>a</sup> (pH 8.4, 24 min), (1/50,)	30 min, 37 °C
NR1D2	CC1 <sup>a</sup> (pH 8.4, 24 min)	1 h, 37 °C

<sup>a</sup> CC1: ethylenediaminetetraacetic acid (EDTA)-based heat-induced antigen retrieval; <sup>b</sup> Ribo CC o CC2, citrate-based heat-induced enzyme retrieval.

**Table S2.** Relationship between expression levels of circadian proteins and development of MM after disease diagnosis of individuals included in the study.

		PER1			PER2			PER3			CRY2			BMAL1			NR1D2		
		Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>
All patients	No	59 (37.8)	97 (62.2)	ns	52 (33.3)	104 (66.7)	ns	142 (90.4)	15 (9.6)	ns	12 (7.6)	145 (92.4)	ns	21 (13.5)	134 (86.5)	ns	92 (59.0)	64 (41.0)	ns
	Yes	17 (43.6)	22 (56.4)		16 (40.0)	24 (60.0)		38 (90.5)	4 (9.5)		2 (4.8)	39 (95.2)		6 (15.0)	34 (85.0)		21 (52.5)	19 (47.5)	
3 years after disease diagnosis	No	60 (37.0)	102 (63.0)	ns	54 (33.1)	109 (66.9)	ns	147 (89.6)	17 (10.4)	ns	12 (7.3)	152 (92.7)	ns	20 (12.3)	142 (87.7)	ns	95 (58.3)	68 (41.7)	ns
	Yes	14 (48.3)	15 (51.7)		12 (41.4)	17 (58.6)		29 (93.5)	2 (6.5)		0 (0.0)	30 (100.0)		6 (20.7)	23 (79.3)		16 (55.2)	13 (44.8)	
5 years after disease diagnosis	No	56 (37.6)	93 (62.4)	ns	50 (33.6)	99 (66.4)	ns	133 (88.7)	17 (11.3)	ns	11 (7.3)	139 (92.7)	ns	19 (12.7)	130 (87.2)	ns	88 (59.1)	61 (40.9)	ns
	Yes	15 (42.9)	20 (57.1)		15 (41.7)	21 (58.3)		36 (94.7)	2 (5.3)		1 (2.7)	36 (97.3)		6 (16.7)	30 (83.3)		20 (55.6)	16 (44.4)	

<sup>a</sup>  $\chi^2$  or Fisher's exact tests.

**Table S3.** Relationship between expression levels of circadian proteins and development of LR after disease diagnosis of patients included in the study.

		PER1			PER2			PER3			CRY1			CRY2			BMAL1		
		Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>	Low	High	<i>p</i> <sup>a</sup>
All patients	No	73 (38.8)	115 (61.2)	ns	69 (36.5)	120 (63.5)	ns	171 (90.0)	19 (10.0)	ns	58 (30.7)	131 (69.3)	ns	14 (7.4)	176 (92.6)	ns	30 (16.0)	158 (84.0)	ns
	Yes	12 (42.9)	16 (57.1)		12 (42.9)	16 (57.1)		29 (100.0)	0 (0.0)		6 (20.7)	23 (79.3)		1 (3.4)	28 (96.6)		3 (10.7)	25 (89.3)	
3 years after disease diagnosis	No	75 (39.5)	115 (60.5)	ns	69 (35.9)	123 (64.1)	ns	173 (89.6)	20 (10.4)	ns	59 (30.7)	133 (69.3)	ns	15 (7.8)	178 (92.2)	ns	27 (14.1)	164 (85.9)	ns
	Yes	9 (40.9)	13 (59.1)		10 (47.6)	11 (52.4)		22 (100.0)	0 (0.0)		4 (18.2)	18 (81.8)		0 (0.0)	22 (100.0)		3 (14.3)	18 (85.7)	
5 years after disease diagnosis	No	69 (39.7)	105 (60.3)	ns	64 (36.3)	111 (63.7)	ns	155 (88.6)	20 (11.4)	ns	55 (31.4)	120 (68.6)	ns	14 (8.0)	162 (92.0)	ns	26 (14.9)	148 (85.1)	ns
	Yes	11 (40.7)	16 (59.3)		13 (48.1)	14 (51.9)		28 (100.0)	0 (0.0)		7 (25.0)	21 (75.0)		1 (3.6)	27 (96.4)		3 (11.1)	24 (88.9)	

<sup>a</sup>  $\chi^2$  or Fisher's exact tests.