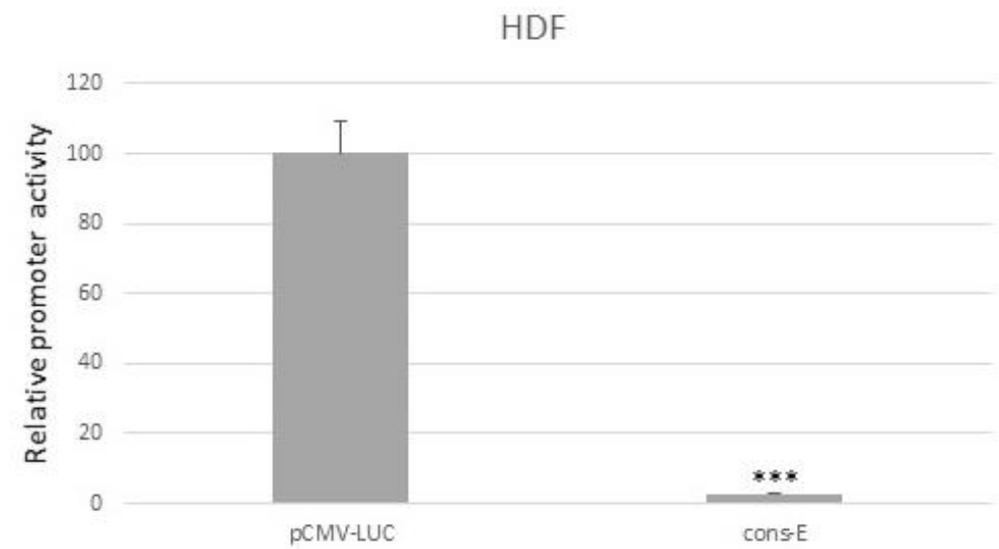
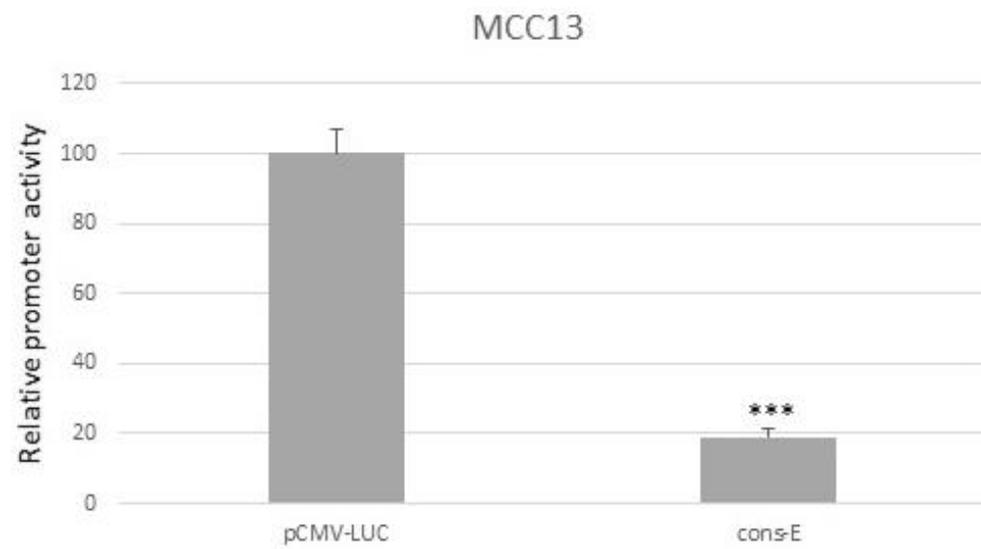
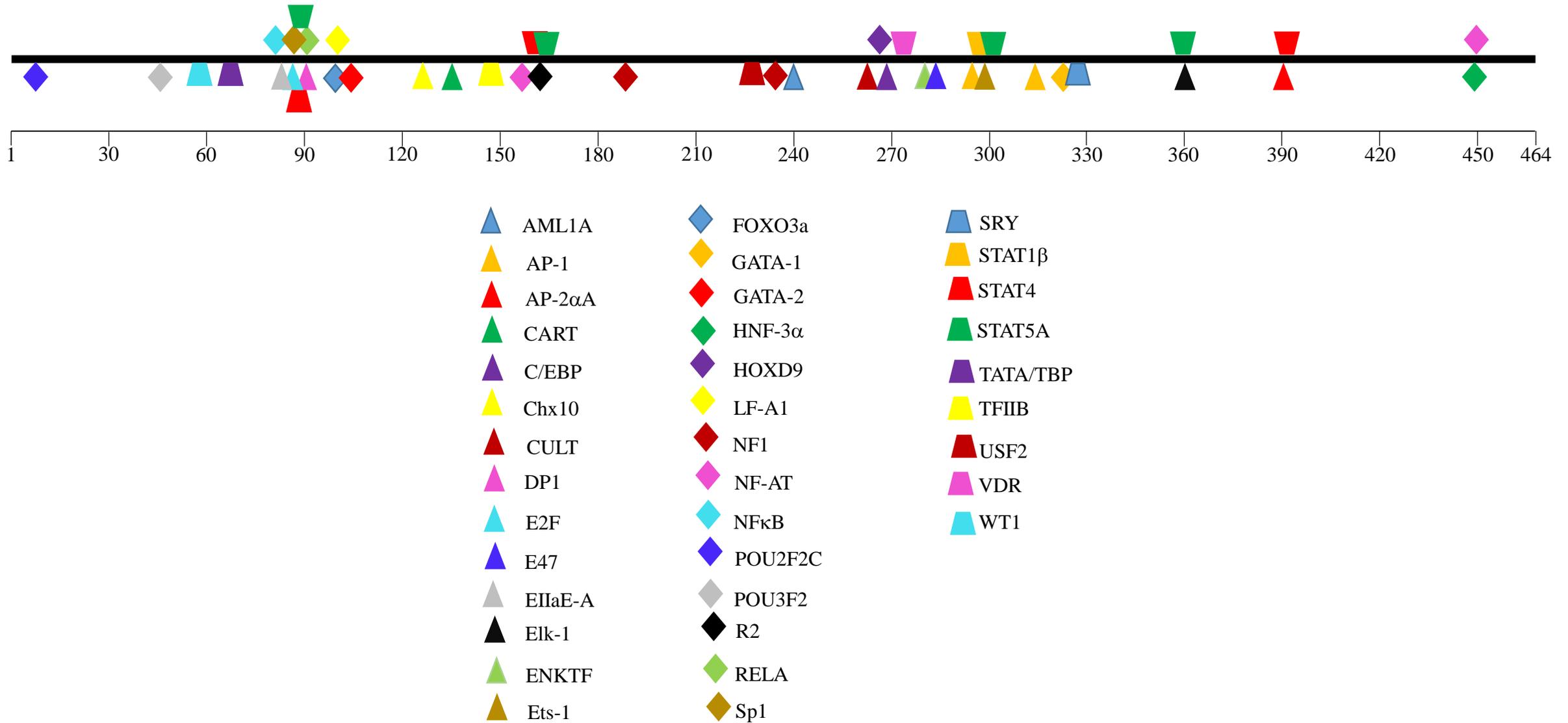


Supplementary Figure S1. Early and late promoter activity of seven MCPyV NCCR variants in MCC13 and human dermal fibroblasts. Promoter activities were determined by transient transfection studies with a luciferase reporter gene and are were corrected for the protein content in each sample. Promoter activity is expressed as relative luciferase activity (RLU).



Supplementary Figure S2. Relative promoter activity of the immediately early cytomegalovirus and the consensus early MCPyV promoter in MCC13 and human dermal fibroblasts (HDF).

Supplementary Figure S3. Putative transcription factor binding sites in the consensus MCPyV NCCR. See Supplementary Table 4 for details.



Supplementary Table S1. Detection of MCPyV in benign and diseased human tissues other than Merkel cell carcinoma.

System	Benign	Reference	Diseased	Reference	
Circulatory system	Blood, plasma or serum from healthy donors	[1-8]	Cutaneous T- and B-cell lymphoma	[14-16]	
	Sera from HIV-negative patients	[9]	Pseudolymphoma	[14]	
	PBMC ^a healthy donors	[3]	Blood from a patient with Stevens-Johnson syndrome	[17]	
	Whole blood from immunocompetent individuals	[10-12]	Blood from chronic lymphocytic leukemia patients	[2, 4, 8, 18-22]	
	Heart		[10, 13]	Blood renal transplant patients	[23, 24]
				Inflammatory monocytes	[25]
				Blood MCC patients	[26]
				Blood from an acute myeloid leukemia patient	[27]
				Sera from HIV-positive patients	[9]
				PBMC from patients with Langerhans cell histiocytosis	[28]
				Non-Hodgkin lymphoma	[29, 30]
				Hodgkin lymphoma	[29]
				Whole blood from breast cancer patients	[31]
				Whole blood from immunocompromised patients	[12]
Sera of AML ^b and ALL patients who underwent hematopoietic stem cell transplantation	[32]				
Blood polytransfused patients with hematological diseases	[8]				
Digestive system	Saliva	[33-37]	Oral mucosa HIV-positive men	[26]	
	Mouthwash healthy individuals	[38]	Colon cancer	[33, 39]	

Oral tissue/mucosa	[33, 35]	Liver from patients with cirrhosis	[10, 13, 33]
Feces children	Li K ^c	Liver cancer	[10, 13, 33]
Healthy colon tissue	[33, 39]	Anal cancer sample	[26]
Stomach	[10, 13]	Anal mucosal samples HIV-positive men	[26]
Liver	[10, 13, 33]	SCC ^d oral cavity	[33, 44, 45]
Small intestine	[10, 13, 40]	SCC larynx	[46]
Hemorrhoid	[40]	SCC esophagus	[33, 41, 42]
Gall bladder	[13, 40]	Tumors of the salivary gland, including Warthin's tumor	[30, 47]
Appendix	[40]	Head and neck cancer of throat, tongue, cheek, outer ear, larynx, mandibular	[48]
Pancreas	[13]	Small cell cancer of the parotid	[49]
Esophagus	[13, 33, 41, 42]	Oral tissue renal transplant patients	[34]
Oral tissue	[34]	Oral and jaw tumors	[30]
Salivary gland	[43]	Oral mucosa from patients with Langerhans cell histiocytosis	[28]
		Juvenile nasopharyngeal angiofibroma	[45]
		Feces thalassemic patients	[50]
		Feces acute myeloid leukemia patients	[50]
		Pleomorphic adenoma	[43]
		Warthin's tumor	[43]

			Salivary gland adenocarcinoma	[43]
Endocrine system	Adrenal gland	[13]	Pituitary from patients with Langerhans cell histiocytosis	[28]
	Thyroid gland	[13]		
Excretory System	Urine healthy	[23, 51-53]	Urine renal transplant patients	[23, 24, 51-53]
	Urine bladder	[10, 13, 33]	Urine or tumor tissue of bladder cancer patients	[10, 13, 33, 54]
	Kidney	[10, 13]	Renal carcinoma	[33]
			Urine patients with orthopedic disorder, acute surgical conditions or ear, nose, skin and dental disorder	[54]
Integumentary system	Normal skin/cutaneous swabs	[13, 16, 40, 55-70]	Skin psoriasis patient	[26, 33, 59, 66, 78]
	Skin from patients with Verruca vulgaris	[71-73]	Actinic porokeratosis	[78, 79]
	Eyebrow hairs	[26, 61, 68, 69, 74-76]	Actinic keratosis	[73, 80-82]
	Inner root sheath cells of hair follicles	[77]	Skin lesions from chronic lymphocytic leukemia patients	[75]
			Skin from patients with Langerhans cell histiocytosis	[28]
			Skin patient with epidermodysplasia verruciformis	[83, 84]
			Verrucous papilloma of the skin	[85]
			Cutaneous swabs forehead of HIV-positive patients	[60]
			Skin patients with bullous pemphigoid	[59]
			Skin patients with cutaneous drug side-effect	[59]
			Skin from patients with seborrheic keratosis	[71, 86, 87]

			Skin from patient with pruritic dermatosis	[88]
			Atopic dermatitis	[66]
			Palmoplantar pustulosis	[66]
			Skin from patients with mycosis fungoides	[15, 16, 59, 89]
			Fullicotropic mycosis fungoides (cutaneous T-cell lymphoma)	[90]
			Skin from T-cell mediated skin benign infiltrate	[66]
			Sézary syndrome	[15, 89]
			Fluid skin lesion Stevens-Johnson syndrome	[17]
			Kaposi's sarcoma	[40, 59, 78, 91, 92]
			Melanoma	[93]
			Cutaneous SCC	[28, 33, 38, 65, 67, 70, 72, 73, 76, 79, 82, 93-102]
			Bowen's disease	[71, 79, 94]
			Atypical fibroxanthoma	[82, 103]
			Porocarcinoma (cancer of the sweat glands)	[63, 65]
			Dermatofibrosarcoma protuberans	[79, 104]
			Keratoacanthoma	[79, 95]
			BCC ^e	[36, 70, 79, 81, 82, 93, 94, 105-107]
			Langerhans cell sarcoma	[108]

			Trichoblastoma	[105]
			SCC of the skin	[107, 109]
			Spitz naevus	[110]
			Non-melanoma skin cancer (including BCC, SCC, actinic keratosis, Bowen's disease)	[111]
			Fanconi anemia-associated head and neck SCC	[112]
Lymphatic system	Lymph nodes	[29]	Tonsillar SCC	[114, 115]
	Lymphoid tissue	[113]	Epithelial thymic tumors	[119]
	Bone marrow	[13]		
	Spleen	[13]		
	Tonsils	[1, 37, 114-118]		
	Adenoid tissue	[116]		
Nervous system	Brain	[10]	CNS tumors	[30, 120]
Reproductive system	Prostate	[13]	Prostatic secretion prostate cancer patients	[123]
	Cervix	[121]	Prostate cancer	[33, 124]
	Ovary	[10]	Cervical SCC carcinoma	[125, 126]
	Placenta	[122]	Cervical adenocarcinoma	[125, 126]
	Testis	[13]	Undifferentiated carcinomas of the cervix	[126]
	Vagina, cervix, vulvar skin, anus from immunodeficient patient with WILD syndrome	[26]	Breast cancer	[31, 127-130]

	(warts, immunodeficiency, lymphedema, anogenital dysplasia)		Benign breast disease	[31]
			Testical cancer tissue (seminoma)	[33]
			Penile mucosal HIV-positive men	[26]
Respiratory system	NPA ^e	[1, 113, 131-135]	NPA from patients with infectious diseases, hematology disorder, intensive care or cardiac or thoracic disease	[137]
	lung	[10, 17, 33, 136]	NPA of renal transplant patients	[23]
			NPA of cystic fibrosis patients	[138]
			Non-small cell lung cancer	[101, 139-144]
			SCC of the lung	[100, 140, 145]
			Adenocarcinoma	[100, 140-145]
			Large-cell neuroendocrine carcinoma	[100]
			Pleomorphic carcinoma	[100]
			Bronchoalveolar carcinoma	[141]
			Lung cancer (not specified)	[33]
			Small cell lung cancer	[139, 146]
			Extrapulmonary small cell carcinoma	[147]
			Mesothelioma	[148]
Skeletal system			Bone from patients with Langerhans cell histiocytosis	[28]
			Ewing sarcoma	[102]

^ePeripheral blood mononuclear cell

^bAcute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL)

^cDirect submission Li K

^dSquamous cell carcinoma

^eBasal cell carcinoma

^fNasopharyngeal aspirates

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Supplementary Table S2. MCPyV isolated in sewage water and environmental surfaces.

Source	Sequence MCPyV genome	reference
Sewage and river water (Brazil, Italy, Argentina, Uruguay)	Not done	[1-5]
	M-cg-9-11.1	[6]
	M-cg-9-11.3	[6]
	M-cg-28-8.1	[6]
	M-cg-28-8.16	[6]
Swimming pool	Not done	[7]
Environmental surfaces at lab and home (e.g. door handles, tv remote control, computer keyboard and mouse, etc)	Not done	[8]

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Supplementary Table S3. MCPyV NCCR variants and mutations compared to the consensus sequence.

Variant (accession number)	Group	NCCR^a	Source	Reference
R06b (HM011538)	2	ins369AACTC	healthy facial skin	[1]
R09b (HM011539)	1	ΔT168	healthy facial skin	[1]
R10b (HM011540)	5	C51T, A251C, ins372ACAAC, Δ381-387AACAAGG, T449C	healthy facial skin	[1]
R12a (HM011541)	1	consensus	healthy facial skin	[1]
R12b (HM011542)	1	insA213	healthy facial skin	[1]
R13a (HM011543)	1	ΔAA221-222	healthy facial skin	[1]
R14a (HM011544)	2	ins369AACTC	healthy facial skin	[1]
R14b (HM011544)	2	ins369AACTC	healthy facial skin	[1]
R15a (HM011546)	4	Δ105-112CCTTAGAT	healthy facial skin	[1]
R15b (HM011547)	4	Δ105-112CCTTAGAT	healthy facial skin	[1]
R16b (HM011548)	6	A234T, ins373CAAC, insT379, insAA383, T449C	healthy facial skin	[1]
R17a (HM011555)	1	ΔT168	healthy facial skin	[1]
R17b (HM011556)	1	consensus	healthy facial skin	[1]
R18b (HM011550)	1	consensus	healthy facial skin	[1]
R20b (HM011551)	1	consensus	healthy facial skin	[1]
R25b (HM011552)	2	CT13T, ins369AAC	healthy facial skin	[1]
R26b (HM011553)	1	C272T, Δ392C	healthy facial skin	[1]
R30a (HM011557)	1	consensus	healthy facial skin	[1]
R30b (HM011554)	1	consensus	healthy facial skin	[1]
124/Sweden (KX827417)	1	consensus	blood AML patient	[2]
7673/2011/HUN (KC202810)	3	T102A, ins372TCAAT	MCC	[3]
915F 06 001 PJ2 (JQ479315)	1	consensus	healthy facial skin	[4]
915F 06 002 KN4 (JQ479316)	2	ins369AACTC	healthy facial skin	[4]
915F 06 005 FS2 (JQ479318)	1	consensus	healthy facial skin	[4]
915F 06 004 BG1 (JQ479317)	1	C6G	healthy facial skin	[4]
915F 06 007 FD3 (JQ479319)	1	consensus	healthy facial skin	[4]

915F 06 008 CG4 (JQ479320)	2	ins369AACTC	healthy facial skin	[4]
AiDo (KJ128376)	1	consensus	MCC	[5]
AmePI (KF266965)	1	Δ T379, insT401, T449C	healthy facial skin	[6]
BroLi (KJ128377)	1	consensus	MCC	[5]
CVG-1 (MH136801)	1	consensus	MCC	[7]
DyskA (KX781279)	1	consensus	swab from normal skin	[8]
EuroCauC1 (KF266963)	1	G363A	healthy facial skin	[6]
FraMerk2 (JN383838)	1	Δ G300	MCC	[9]
FraMerk20 (JN383839)	1	insA213, G301A, Δ A304, G309A, G363A	MCC	[9]
FraMerk22 (JN383840)	1	G143T, C170T, C176T, G188A, G363A	MCC	[9]
FraMerk24 (JN383841)	1	G96A, G300T	MCC	[9]
HB039C (KC571692)	6	A234T, ins373CAAC, insT379, insAA383, T449C	Feces children	unpublished ^b
HF (JF813003)	1	consensus	MCC	[10]
KIB (MK561422)	7	A234T, ins372TCAAC, ins38AA, ins429TTTCTCTTACAAAGGGAGGAGACA	Blood healthy volunteer	[11]
LoKe (KJ128381)	1	consensus	MCC	[5]
M-cg-9-11.1 (MG241579)	2	ins369AACTC, insT401, T449C	sewage sample	[12]
M-cg-9-11.3 (MG241580)	2	Ins369AACTC	sewage sample	[12]
M-cg-28-8-1 (MG241581)	1	A361G	sewage sample	[12]
M-cg-28-8.16 (MG241582)	1	Δ A222	sewage sample	[12]
MCC85 (JF813002)	1	C372G	MCC	[10]
MCC339 (EU375804)	2	ins369AACTC	MCC	[13]
MCC344 (JF812999)	2	ins369AAC	MCC	[10]
MCC349 (JF813000)	1	consensus	MCC	[10]
MCC350 (EU375804)	1	G32C, G152T, G363A	MCC	[13]
MCC352 (JF813001)	1	consensus	MCC	[10]
MCVw156 (HM355825)	1	G32C, Δ A222	MCC	unpublished ^c
MKL-1 (FJ173815)	1	T52C	MCC	[14]
MKT-21 (FM865403)	2	ins369AACTC	MCC	[15]
MKT-22 (FM865404)	1	T94C, Δ T408, C448A	MCC	[15]
MKT-23 (FM864208)	2	G143A, C145T, C158T, A173G, ins369AACTC	MCC	[15]
MKT-26 (FM865405)	1	T86C, T210C, Δ A222, A435G	MCC	[15]
MKT-32 (FM995609)	1	T146C, Δ G274	MCC	[15]
MS-1 (JX045709)	2	ins369AACTC	MCC	[13]
OcepolW1 (KF266964)	5	T5G, C26A, G40A, T108G, ins372372ACAA, Δ 381-387AACAAGG, C393T, T449C	Swab healthy skin	[6]
PeTa (KJ128378)	2	ins369AACTC	MCC	[5]

TKS (FJ464337)	6	A234T, ins373CAAC, insT379, insAA383, T449C	Kaposi's sarcoma	[16]
WaGa (KJ128379)	1	consensus	MCC	[5]
WoWe (KJ128380)	1	consensus	MCC	[5]

^aThe numbers refer to the nucleotide of the consensus NCCR

^bdirect submission by Li et al., 2013.

^cdirect submission by Carter JJ et al., 2010 and Cahill and Paulson, 2010.

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Supplementary Table S4. Putative consensus transcription factor binding motifs in the consensus MCPyV NCCR.

Transcription factor	Consensus motif	Motif in MCPyV NCCR	NCCR variants tested in this study with mutation in putative motif
AML1A	ACCACAAAAT	<u>AAGTTGTGGT</u> (238-247)*	
AP-1/c-JUN	TGACTCA	TGACTCA (287-293) and TGACT <u>G</u> A (314-320)	
AP-2 α A	GCAGGC	GGAGGC (387-392)	10b (Δ 381-387)
Cart-1	AATTA	AATTA (128-132)	
C/EBP α/β	TTGCTC	TTGCT <u>G</u> (266-271)	
Chx10	^A / _T T ^A / _T GCTAATTA	TTTGCTAATTA (122-132)	
CUTL1	ATTG <u>G</u> T	ATTGCT (265-270)	
DP1	ATTTCCCGCC	<u>G</u> TTTCCCGCC (88-92)	
E2F-1	TCCCGCC	TCCCGCC (86-92)	
E2F-5	TTTCGCGC	TTT <u>C</u> CGC (84-91)	
E47	ATCTGGC	TTCTGGC (278-284)	
EIIaE-A	CGCCCTC	CGCCCT <u>T</u> (89-95)	
Elk-1	GGAAG	GGAAG (359-363)	
ENKTF-1	TGGCG ^C / _T ^A / _T G	TGGC <u>A</u> TTG (281-288)	
c-Ets-1	CTTCCTG	<u>T</u> TCCTG (294-300)	
c-Ets-2	AGGAAATG	CATTCCT (299-292)#	
FOXO3A	CTTAAATA	CTTAGATA (106-113)	
GATA-1	GATAAG	GATA <u>A</u> A (319-324)	
GATA-2	GCC ^C / _T TATCT	AGATACT <u>G</u> C (109-117)	
HNF-3 α	AAGTAAATAA	TTATTTA <u>T</u> TT (458-449)	10b (T449C), 16b (T449C)
HOXD9	AATAAAAAATA	<u>A</u> ACTTTTATT (267-258)	
LF-A1	TGCCCTG	TGCCCT <u>I</u> (102-108)	15a (Δ 105-112); HUN (T102A)
NF1	TTGGC	GCCAA (208-204) and GCCAA (239-235)	
NF-AT	AATTTTCC	<u>T</u> TTTTTCC (162-179)	

NF-AT3	T ^A / _T A ^A / _T TTTTCC	TTTTTTTTCC (161-170)	
NF-AT4	A ^A / _T TTATTTTTCC	ATTTATTTTTCA (451-462)	
NF-κB	TGGGAATTTCC	CTGCAGTTTCC (88-78)	
POU2F2C	ATGCAAAT	ATGCAGAAG (10-17)	
POU3F2	AAATGAA	AAATGAG (44-50)	
R2	TCCAAC	TCCAGA (168-173)	
RELA	CAGATTTCCC	CAGTTTCCC (81-90)	
Sp1	G ^G / _T GGGCGGG	CCCGCCCC (94-87)	
SRY	AAACAA ^A / _T	AAACAAA (322-328)	
STAT1β	ATTTCCAAGA	ATTTCTGGA (293-302)	
STAT4	ATTTCC	GTTTCC (83-88), TTTTCC (165-170), ATTTCC (293-298)	
STAT5A	GGAA	TTCC (85-88, 167-170, 295-298) and GGAA (359-362)	
TBP/TFIID	TATAAAAA	TTTTTATA (77-70)	
TFIIB	GTCTCAGA	GCCTCAGA (143-150)	
USF2	CAGGTGACC	AGTCACCTA (230-222)	
VDR	GGGT	GGGT (274-277)	
WT1	GTGTGTG	ACCTCAC (59-53)	

*Numbers refer to position in the consensus NCCR.

#On the complementary strand

The ALLGEN PROMO transcription factor prediction database was used [1,2]. Motifs with none, one (motif <6 base-pairs) or 2 (motifs >6 base-pairs) mutations compared to the consensus binding site in the MCPyV NCCR are shown.

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