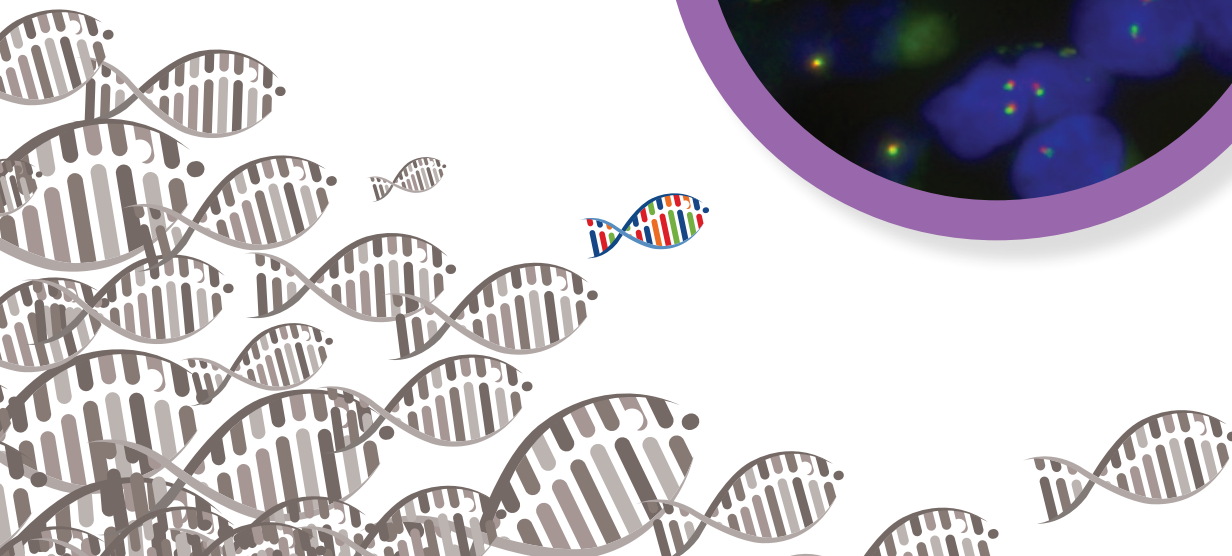
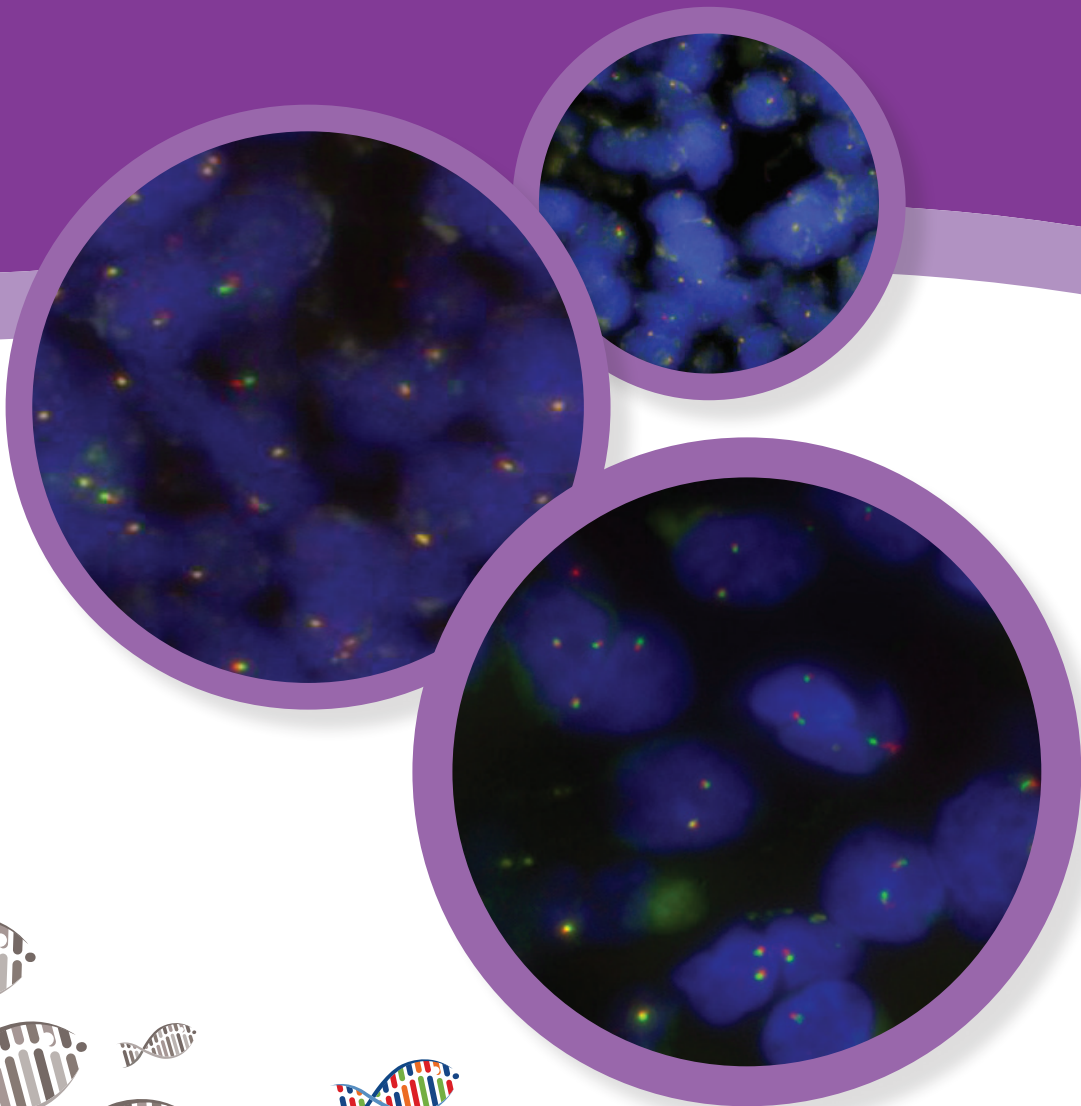


# New Pathology Probes for 2017



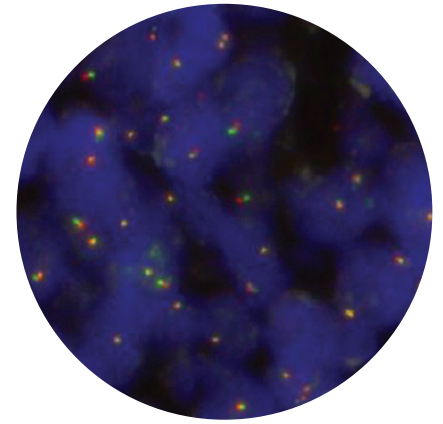
## FUS Breakapart Probe

The *FUS* (*FUS RNA binding protein*) gene at 16p11.2 is a member of the FET family of protein-encoding genes, closely-related to the *EWSR1* (*EWS RNA binding protein 1*) gene<sup>1</sup>.

Recurrent rearrangements involving the *FUS* gene with a number of different partner genes have been reported in various types of neoplastic disease, notably soft tissue sarcomas and acute myeloid leukaemia. In some tumour types *FUS* and *EWSR1* may replace each other as fusion partners<sup>2</sup>.

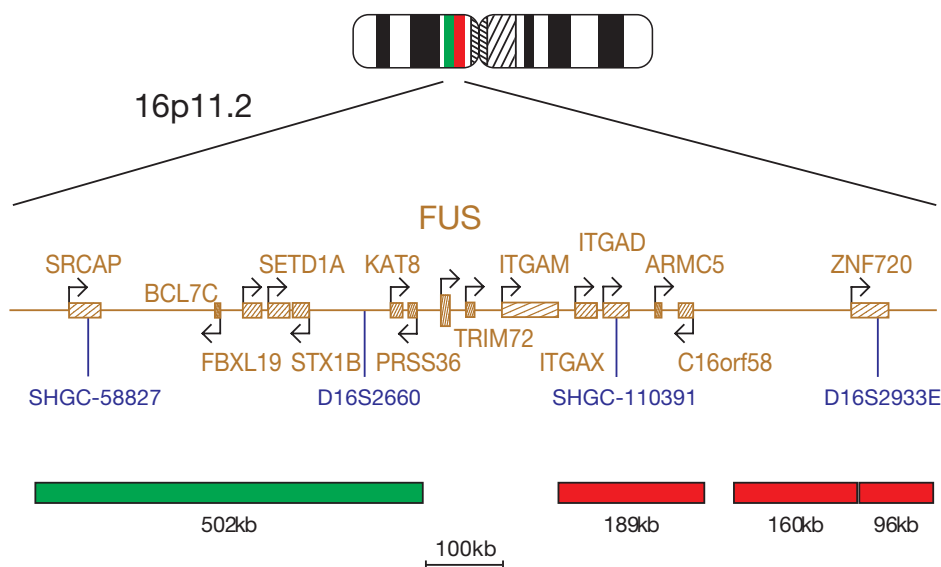
In soft tissue sarcoma, approximately 90% of cases of myxoid liposarcoma are characterised by the presence of a *FUS-DDIT3* rearrangement arising from a t(12;16)(q13;p11) translocation<sup>3,4</sup>; the *FUS-CREB3L1* and the *FUS-CREB3L2* fusions, resulting from t(11;16)(p11;p11) and t(7;16)(q32-34;p11) translocations respectively are characteristic of low-grade fibromyxoid sarcoma<sup>5</sup>, whereas the t(12;16)(q13;p11) translocation resulting in a *FUS-ATF1* fusion gene is seen in angiomatoid fibrous histiocytoma<sup>6</sup>.

This breakapart probe has been designed to allow detection of *FUS* rearrangements regardless of the partner gene involved.



### References:

1. Göransson, M. *et al.*, *Oncogene* 2009. 28:270–278
2. Andersson, M.K. *et al.*, *BMC cell biology* 2008. 9:37
3. Willeke, M. *et al.*, *Clin Cancer Res.* 1998. 4:1779–1784
4. Panagopoulos, I. *et al.*, *Cancer Research* 1994. 54:6500–6503
5. Mertens, F. *et al.*, *Laboratory investigation* 2005. 85:408–15
6. Tanas, M.R. *et al.*, *Modern pathology* 2010. 23:93–7



## FOXO1 Breakapart Probe

Translocations involving the FOXO1 (*forkhead box O1*) gene at 13q14.1 and either the PAX3 (*paired box 3*) gene at 2q36.1 or the PAX7 (*paired box 7*) gene at 1p36.1 are seen frequently in cases of alveolar rhabdomyosarcoma<sup>1,2</sup>.

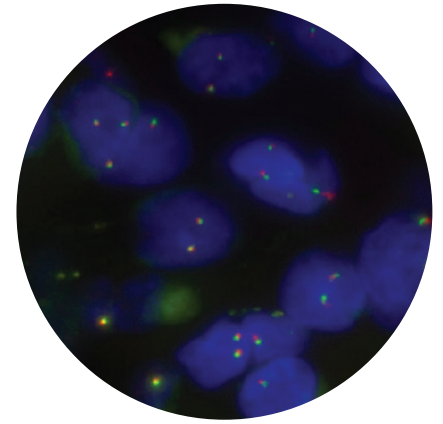
Rhabdomyosarcoma is the most common soft-tissue sarcoma seen in children and younger adults with two major histological subtypes: alveolar rhabdomyosarcoma (ARMS) and embryonal rhabdomyosarcoma (ERMS)<sup>3</sup>. FOXO1 rearrangements are recognised recurrent abnormalities seen in ARMS, but not seen in ERMS<sup>1,2</sup>.

Approximately 55% of cases of ARMS are associated with a PAX3-FOXO1 rearrangement via a t(2;13)(q36.1;q14) translocation and 22% of cases of ARMS are associated with a PAX7-FOXO1 rearrangement via a t(1;13)(p36;q14) translocation<sup>4</sup>. These translocations lead to the fusion of transcription factor FOXO1 to the transcription factors PAX3 and PAX7 located at 2q36.1 and 1p36.13 respectively<sup>2</sup>.

Studies have shown that ARMS patients with PAX-FOXO1 rearrangements have an inferior outcome compared to ERMS patients, whereas ARMS patients without PAX-FOXO1 rearrangements show similar outcomes to ERMS<sup>2,5</sup>.

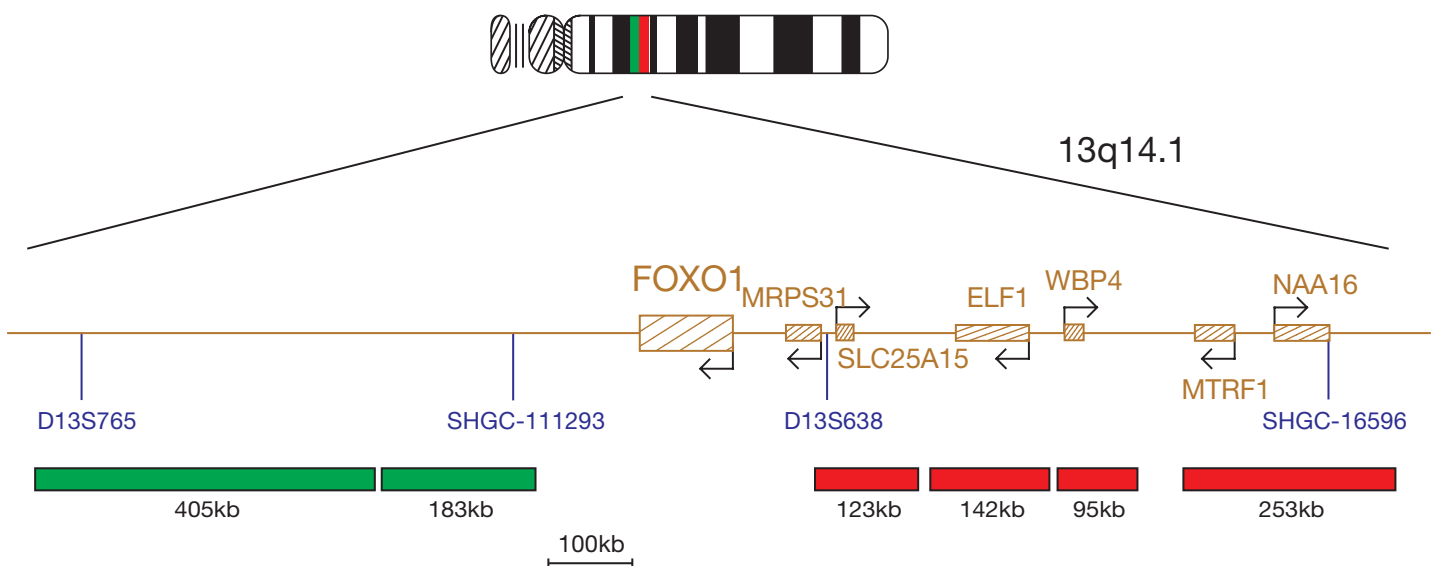
A subset of patients with ARMS may show fusion gene amplification. This is most commonly associated with the presence of PAX7-FOXO1 rearrangements and has been shown to be associated with significantly improved outcome over ARMS patients with PAX-FOXO1 rearrangements without fusion gene amplification<sup>6</sup>.

This breakapart probe design allows the detection of FOXO1 rearrangements, regardless of the partner gene involved.



### References:

1. Anderson *et al.*, Am J Pathol. 2001 Sep;159(3):1089-96
2. Jothi *et al.*, Mol Cancer Ther. 2013 Dec;12(12):2663-74
3. Ognjanovic *et al.*, Cancer 2009; 115(18): 4218-4226.
4. Sorensen *et al.*, J Clin Oncol. 2002;20(11):2672-9
5. Skapek *et al.*, Pediatr Blood Cancer. 2013 Sep;60(9):1411-7
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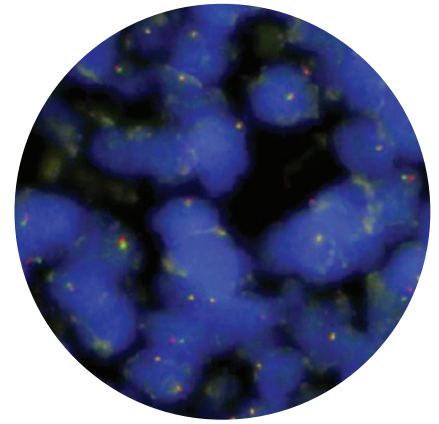
## TFE3 Breakapart Probe\*

TFE3 (*transcription factor binding to IGHM enhancer 3*) is a protein-coding gene located at Xp11.23. Recurrent rearrangements of the TFE3 gene have been reported in a number of neoplastic diseases – often grouped together as ‘Xp11 translocation cancers’ – these include: renal cell carcinoma (RCC), soft tissue alveolar soft part sarcoma (ASPS), perivascular epithelioid cell tumors (PEComa), epithelioid hemangioendotheliomas (EHE) and melanotic Xp11 translocation renal cancer<sup>1,2</sup>.

In RCC, TFE3 translocation partners have been shown to include the ASPSCR1, SFPQ and NONO genes<sup>3</sup>. Although RCC and ASPS have been shown to have identical ASPSCR1-TFE3 fusion transcripts, the t(X;17) translocation is consistently balanced in the former but usually unbalanced in the latter - the derivative X chromosome is not seen in ASPS<sup>4</sup>.

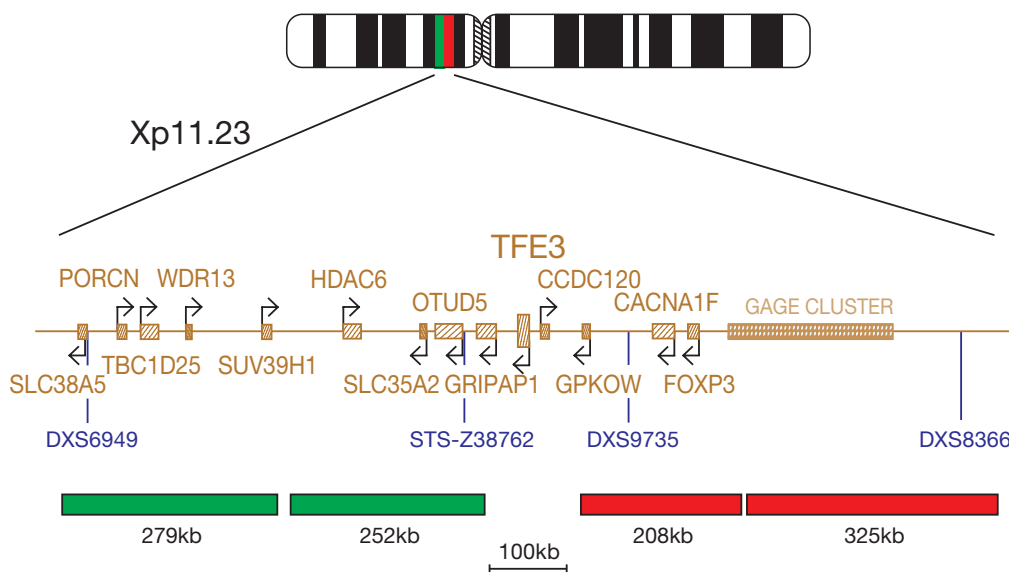
In epithelioid hemangioendothelioma the novel YAP1-TFE3 fusion is seen, and defines a clinically distinct subset of this disease<sup>5,6</sup>, whereas in PEComa, the predominant partner has been shown to be the SFPQ gene<sup>7</sup>.

This research use only (RUO) probe has been designed for the investigation of TFE3 rearrangements, regardless of the partner gene involved.



### References:

1. Eble JN, *et al.*, World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. Lyon: IARC Press; 2004.
2. Wu A *et al.*, Histopathology 2008;53(5):533-44
3. Hodge JC, *et al.*, Mod Pathol 2014 Jan;27(1):113-27.
4. Argani P, *et al.*, Am J Pathol 2001;159(1):179-92.
5. Antonescu CR, *et al.*, Genes, Chromosom Cancer. 2013 Aug;52(8):775-84.
6. Lee SJ, *et al.*, Oncotarget. 2016;7(7):7480-8.
7. Rao Q, *et al.*, Am J Surg Pathol. 2015 Sep;39(9):1181-96



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## Pathology Probe Range

Probe Name	Chromosome Region	Probe Type	Control Probe	No. Tests	Cat. No.*
1p36/1q25 & 19q13/19p13	1p36.32/19q13.33	Deletion	1q25.2/19p13.2	5 or 10	LPS 047
ALK	2p23.2 p23.1	Breakapart	–	5 or 10	LPS 019
CHOP (DDIT3)	12q13.3	Breakapart	–	5 or 10	LPS 015
C-MET (MET)	7q31.2	Amplification	D7Z1	5 or 10	LPS 004
EGFR	7p11.2	Amplification	D7Z1	5 or 10	LPS 003
EML4	2p21	Breakapart	–	5 or 10	LPS 020
EWSR1	22q12.1-q12.2	Breakapart	–	5 or 10	LPS 006
EWSR1/ERG Dual Fusion	21q22.13-q22.2/22q12.1-q12.2	Translocation	–	5 or 10	LPS 008
FGFR1	8p11.23-p11.22	Breakapart/Amplification	D8Z2	5 or 10	LPS 018
FLI1/EWSR1 Dual Fusion	11q24.3/22q12.1-q12.2	Translocation	–	5 or 10	LPS 007
<b>NEW</b> FOXO1	13q14.1	Breakapart	–	5 or 10	LPS 049
<b>NEW</b> FUS	16p11.2	Breakapart	–	5 or 10	LPS 050
HER2 (ERBB2)	17q12	Amplification	D17Z1	5 or 10	LPS 001
MDM2	12q15	Amplification	D12Z1	5 or 10	LPS 016
N-MYC (MYCN)	2p24.3	Amplification	AFF3	5 or 10	LPS 009
PAX3	2q36.1	Breakapart	–	5 or 10	LPS 012
PAX7	1p36.13	Breakapart	–	5 or 10	LPS 013
RET	10q11.21	Breakapart	–	5 or 10	LPS 045
ROS1	6q22.1	Breakapart	–	5 or 10	LPS 022
ROS1 Plus	6q22.1	Breakapart	–	5 or 10	LPS 046
SRD (CHD5)	1p36.31	Deletion	ZNF672	5 or 10	LPS 010
SYT (SS18)	18q11.2	Breakapart	–	5 or 10	LPS 014
<b>NEW</b> TFE3	Xp11.23	Breakapart	–	50µl or 100µl	RU-LPS 051
TMPRSS2/ERG	21q22.2-q22.3/21q22.13-q22.2	Deletion/Breakapart	ERG	5 or 10	LPS 021
TOP2A	17q21.2	Amplification/Deletion	D17Z1	5 or 10	LPS 002
ZNF217	20q13.2	Amplification	DEFB128	5 or 10	LPS 005
<b>Pretreatment Kit</b>	–	–	–	–	<b>LPS 100†</b>

\* for 5 test kit add -S to catalog number, e.g: LPS ###-S

## Haematopathology Probe Range

Probe Name	Chromosome Region	Probe Type	Control Probe	No. Tests	Cat. No.*
BCL2	18q21.33-q22.1	Breakapart	–	5 or 10	LPS 028
BCL6	3q27.3-q28	Breakapart	–	5 or 10	LPS 029
CCND1	11q13.3	Breakapart	–	5 or 10	LPS 030
IGH	14q32.33	Breakapart	–	5 or 10	LPS 032
IGH/BCL2 Dual Fusion	14q32.33/18q21.33-q22.1	Translocation	–	5 or 10	LPS 033
IGH/CCND1 Dual Fusion	14q32.33/11q13.3	Translocation	–	5 or 10	LPS 031
IGH/MALT1 Dual Fusion	14q32.33/18q21.31-q21.32	Translocation	–	5 or 10	LPS 034
IGH/MYC Dual Fusion	14q32.33/8q24.21	Translocation	–	5 or 10	LPS 035
IGK	2p11.2	Breakapart	–	5 or 10	LPS 038
IGL	22q11.21-q11.23	Breakapart	–	5 or 10	LPS 039
MALT1	18q21.31-q21.32	Breakapart	–	5 or 10	LPS 017
MYC	8q24.21	Breakapart	–	5 or 10	LPS 027
P16 (CDKN2A)	9p21.3	Deletion	D9Z3	5 or 10	LPS 036
P53 (TP53)	17p13.1	Deletion	D17Z1	5 or 10	LPS 037
RB1	13q14.2	Deletion	LAMP1	5 or 10	LPS 011

\* for 5 test kit add -S to catalog number, e.g: LPS ###-S

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990224\_V001/2016

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