

Supplementary Files

Supplementary Table 1. Summary of the most prevalent fusion transcript variants in the literature

Supplementary Table 2. Spreadsheet showing differential gene expression of *EWSR1-ATF1*-rearranged clear cell sarcoma compared to other tumor types compared to other tumor types identified on the Affymetrix platform (1.5 log₂ fold change and *P*-value 0.01).

Supplementary Table 3. Spreadsheet showing differential methylation of *EWSR1-ATF1* rearranged clear cell sarcoma compared to other tumor types identified on the 850k platform (4 log₂ fold change and *P*-value 0.01).

Supplementary Figure 1. Recurrent genetic alterations by *EWSR1/FUS* fusion partner type (*ATF1*, *CREB1*, *CREM*).

Supplementary Figure 2. Heatmap showing differential gene expression of *EWSR1-ATF1*-rearranged clear cell sarcoma compared to other tumor types compared to other tumor types identified on the Affymetrix platform (1.5 log₂ fold change and *P*-value 0.01).

Supplementary Figure 3. Heatmap showing differential methylation of *EWSR1-ATF1* rearranged clear cell sarcoma compared to other tumor types identified on the 850k platform (4 log₂ fold change and *P*-value 0.01).

Supplementary Table 1. Summary of the most prevalent fusion transcript variants in the literature

Reference	Fusion transcript variant
Angiomatoid fibrous histiocytoma (AFH)	
Waters 2000	1 <i>FUS</i> ex5- <i>ATF1</i> ex5
Raddaoui 2002	1 <i>FUS</i> ex5- <i>ATF1</i> ex5
Hallor 2005	1 <i>EWSR1</i> ex7- <i>ATF1</i> ex5
Antonescu 2007	1 <i>EWSR1</i> ex7- <i>ATF1</i> ex5; 8 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Rossi 2007	1 <i>EWSR1-ATF1</i> ; 13 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Yoshida 2019	8 <i>EWSR1-CREB1</i> ; 3 <i>EWSR1-CREM</i> (extracranial myxoid AFH)
Summary:	3 <i>EWSR1-ATF1</i> (2 ex7-ex5); 29 <i>EWSR1-CREB1</i> (21 ex7-ex7); 3 <i>EWSR1-CREM</i> ; 2 <i>FUS</i> ex5- <i>ATF1</i> ex5
Current study:	14 <i>EWSR1-ATF1</i> (3 ex7-ex5; 1 ex7-ex7); 21 <i>EWSR1-CREB1</i> (3 ex7-ex7); 1 <i>EWSR1-CREM</i>
Clear cell sarcoma	
Antonescu 2002	11 <i>EWSR1</i> ex8- <i>ATF1</i> ex4
Panagopoulos 2002	8 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 4 <i>EWSR1</i> ex7- <i>ATF1</i> ex5; 1 <i>EWSR1</i> ex10- <i>ATF1</i> ex5
Coindre 2006	24 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 32 <i>EWSR1</i> ex7- <i>ATF1</i> ex5
Hisaoka 2008	25 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 11 <i>EWSR1</i> ex7- <i>ATF1</i> ex5; 4 <i>EWSR1</i> ex10- <i>ATF1</i> ex5; 2 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Wang 2009	13 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 6 <i>EWSR1</i> ex7- <i>ATF1</i> ex5; 1 <i>EWSR1-CREB1</i>
Jakubauskas 2011	1 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 1 <i>EWSR1</i> ex7- <i>ATF1</i> ex5; 1 <i>EWSR1</i> ex7- <i>ATF1</i> ex4; 1 <i>EWSR1</i> ex9- <i>ATF1</i> ex4;
Segawa 2018	3 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 1 <i>EWSR1</i> ex8- <i>ATF1</i> ex5; 2 <i>EWSR1</i> ex10- <i>ATF1</i> ex5
Yoshida 2019	31 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 1 <i>EWSR1-CREB1</i> ; 1 <i>EWSR1-CREM</i>
Summary:	178 <i>EWSR1-ATF1</i> (1 ex7-ex4; 54 ex7-ex5; 116 ex8-ex4; 1 ex8-ex5; 1 ex9-ex4; 7 ex10-ex5); 4 <i>EWSR1-CREB1</i> (2 ex7-ex7); 1 <i>EWSR1-CREM</i>
Current study:	34 <i>EWSR1-ATF1</i> (1 ex7-ex4; 3 ex7-ex5; 10 ex8-ex4; 2 ex9-ex4); 5 <i>EWSR1-CREB1</i> (1 ex7-ex7); 1 <i>EWSR1-CREM</i> (1 ex8-ex7)
Clear cell sarcoma-like tumor of the gastrointestinal tract	
Antonescu 2006	3 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Stockman 2012	6 <i>EWSR1-ATF1</i> ; 3 <i>EWSR1-CREB1</i>
Segawa 2018	1 <i>EWSR1</i> ex8- <i>ATF1</i> ex4; 1 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Summary:	7 <i>EWSR1-ATF1</i> (1 ex8-ex4); 7 <i>EWSR1-CREB1</i> (4 ex7-ex7)
Current study:	10 <i>EWSR1-ATF1</i> (1 ex7-ex5; 5 ex8-ex4); 10 <i>EWSR1-CREB1</i> (1 ex6-ex6; 1 ex7-ex6; 1 ex7-ex7)
Malignant epithelioid neoplasm with predilection for mesothelial-lined cavities	
Argani 2020	2 <i>EWSR1-ATF1</i> ; 7 <i>EWSR1-CREM</i> (4 ex7/13/14/15-ex7); 4 <i>FUS-CREM</i> (2 ex8-ex5/7)
Shibayama 2021	2 <i>EWSR1-ATF1</i> ; 1 <i>EWSR1-CREB1</i> ; 1 <i>EWSR1</i> ex11- <i>CREM</i> ex7; 4 <i>FUS-CREM</i> (1 ex10-ex7)
Summary:	4 <i>EWSR1-ATF1</i> ; 1 <i>EWSR1-CREB1</i> ; 8 <i>EWSR1-CREM</i> (5 ex7/11/13/14/15-ex7); 8 <i>FUS-CREM</i> (1 ex8-ex5; 1 ex8-ex7; 1 ex10-ex7)
Current study:	2 <i>EWSR1-ATF1</i> ; 8 <i>EWSR1-CREM</i> ; 4 <i>FUS-CREM</i> (1 ex8-ex5; 1 ex8-ex7)
Mesothelioma	
Desmeules 2017	3 <i>EWSR1-ATF1</i> (1 ex13-ex5); 1 <i>FUS-ATF1</i>
Ren 2021	1 <i>EWSR1</i> ex13- <i>ATF1</i> ex5; 1 <i>EWSR1</i> ex8- <i>ATF1</i> ex4
Ajelerio 2021	1 <i>EWSR1-ATF1</i>
Summary:	6 <i>EWSR1-ATF1</i> (1 ex8-ex4; 2 ex13-ex5); 1 <i>FUS-ATF1</i>
Current study:	7 <i>EWSR1-ATF1</i> (1 ex7-ex5; 1 ex13-ex5); 1 <i>EWSR1-CREM</i> (ex10-ex5)
Myxoid mesenchymal tumor or intracranial (myxoid) AFH-like tumor	
Dunham 2008	1 <i>EWSR1</i> ex8- <i>ATF1</i> ex4
Kao 2017	1 <i>EWSR1-ATF1</i> ; 2 <i>EWSR1-CREB1</i> ; 2 <i>EWSR1-CREM</i> (1 ex15-ex7)
Sciot 2017	1 <i>EWSR1-ATF1</i>
Bale 2018	2 <i>EWSR1-CREB1</i> ; 1 <i>EWSR1-CREM</i>
Gareton 2018	1 <i>EWSR1</i> ex7- <i>CREM</i> ex13
Konstantinidis 2019	1 <i>EWSR1-ATF1</i> ; 1 <i>EWSR1</i> ex8- <i>CREM</i> ex4
Ballester 2020	1 <i>EWSR1-ATF1</i>
Komatsu 2020	1 <i>EWSR1-CREB1</i>
Ward 2020	1 <i>EWSR1-ATF1</i>
Sloan 2021	8 <i>EWSR1-ATF1</i> ; 7 <i>EWSR1-CREB1</i> ; 4 <i>EWSR1-CREM</i> ; 1 <i>FUS</i> ex5- <i>CREM</i> ex7
Tan 2021	1 <i>EWSR1-CREM</i>
Valente Aguiar 2021	1 <i>EWSR1-CREB1</i>
Summary:	14 <i>EWSR1-ATF1</i> (1 ex8-ex4); 13 <i>EWSR1-CREB1</i> ; 10 <i>EWSR1-CREM</i> (1 ex7-ex13; 1 ex8-ex4; 1 ex15-ex7); 1 <i>FUS-CREM</i> (ex5-ex7)
Current study:	1 <i>EWSR1-ATF1</i> ; 2 <i>EWSR1-CREB1</i> ; 2 <i>EWSR1-CREM</i>
Primary pulmonary mesenchymal tumor	
Thway 2011	6 <i>EWSR1</i> ex7- <i>CREB1</i> ex7; 1 <i>EWSR1</i> ex7- <i>CREB1</i> ex8
Matsukuma 2012	1 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Smith 2013	1 <i>EWSR1-CREB1</i>
Jeon 2014	4 <i>EWSR1-CREB1</i> ex7
Yanagida 2017	1 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Prieto-Granda 2017	1 <i>EWSR1-CREB1</i>
Chen 2020	1 <i>EWSR1</i> ex7- <i>CREB1</i> ex7
Koelsche 2020	1 <i>EWSR1</i> ex7- <i>CREB1</i> ex5
Gui 2020	1 <i>EWSR1</i> ex9- <i>ATF1</i> ex5
Summary:	17 <i>EWSR1-CREB1</i> (1 ex7-ex5; 1 ex7-ex8; 10 ex7-ex7); 1 <i>EWSR1-ATF1</i> (ex9-ex5)
Current study:	3 <i>EWSR1-CREB1</i> (1 ex8-ex7)
Hyalinizing clear cell carcinoma	

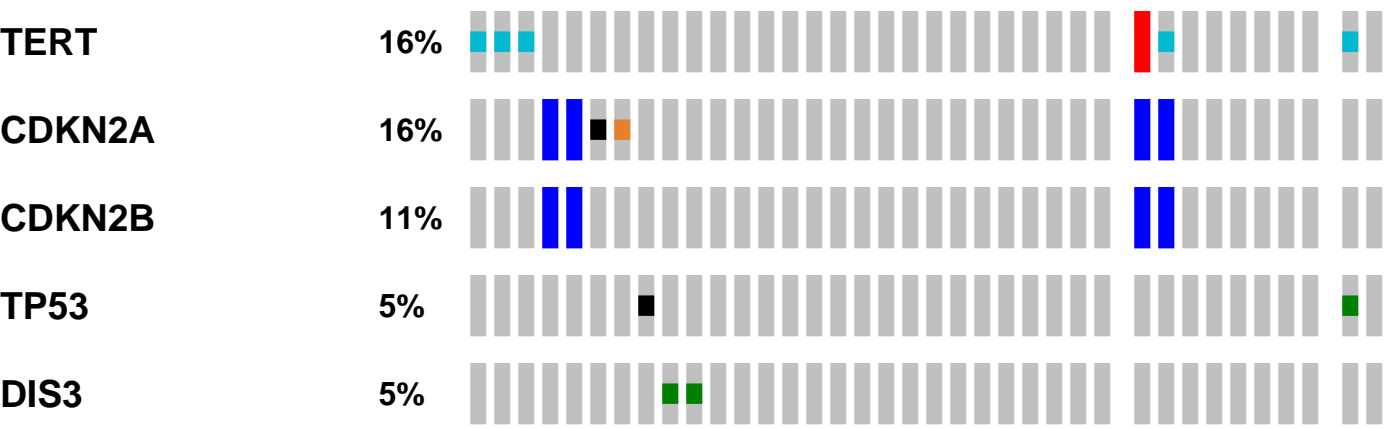
Antonescu 2011	13 <i>EWSR1-ATF1</i> (2 ex11-ex3)
Nakano 2015	2 <i>EWSR1ex11-ATF1ex3</i>
Chapman 2018	2 <i>EWSR1ex13-CREMex6</i> ; 1 <i>EWSR1ex10-CREMex6</i>
Hirose 2020	1 <i>EWSR1ex15-ATF1ex5</i>
Nojima 2021	1 <i>EWSR1ex7/8-ATF1ex4/5</i>
Heft Neal 2021	1 <i>EWSR1ex11-ATF1ex3</i> ; 1 <i>EWSR1ex6-ATF1ex4</i>
Summary:	19 <i>EWSR1-ATF1</i> (1 ex6-ex4; 1 ex7/8-ex4/5; 4 ex11-ex3; 1 ex15-ex5); 3 <i>EWSR1-CREM</i> (1 ex10-ex6; 2 ex13-ex6)
Current study:	10 <i>EWSR1-ATF1</i> (1 ex7-ex4; 1 ex8-ex4; 1 ex9-ex2; 1 ex10-ex3; 3 ex11-ex3)

Clear cell odontogenic carcinoma

Bilodeau 2013	1 <i>EWSR1-ATF1</i>
Yancoskie 2014	1 <i>EWSR1-ATF1</i>
Vogels 2019	2 <i>EWSR1-ATF1</i> ; 1 <i>EWSR1ex7-CREB1ex8</i>
Santana 2020	1 <i>EWSR1-ATF1</i>
Breik 2021	1 <i>EWSR1ex9-CREMex4</i>
Summary:	5 <i>EWSR1-ATF1</i> ; 1 <i>EWSR1-CREB1</i> (ex7-ex8); 1 <i>EWSR1-CREM</i> (ex9-ex4)
Current study:	1 <i>EWSR1-ATF1</i> (ex7-ex4)

Transcripts: *ATF1* (NM_005171); *CREB1* (NM_134442); *CREM* (NM_181571); *EWSR1* (NM_005243); *FUS* (NM_004960).

Number in front of transcript denotes number of cases positive for the fusion. Exon number is indicated whenever available.



Genetic Alteration

- Missense Mutation (putative driver)
- Promoter Mutation
- Splice Mutation (putative driver)
- Truncating Mutation (putative driver)
- Amplification
- Deep Deletion
- No alterations

In group: ATF1

No Yes

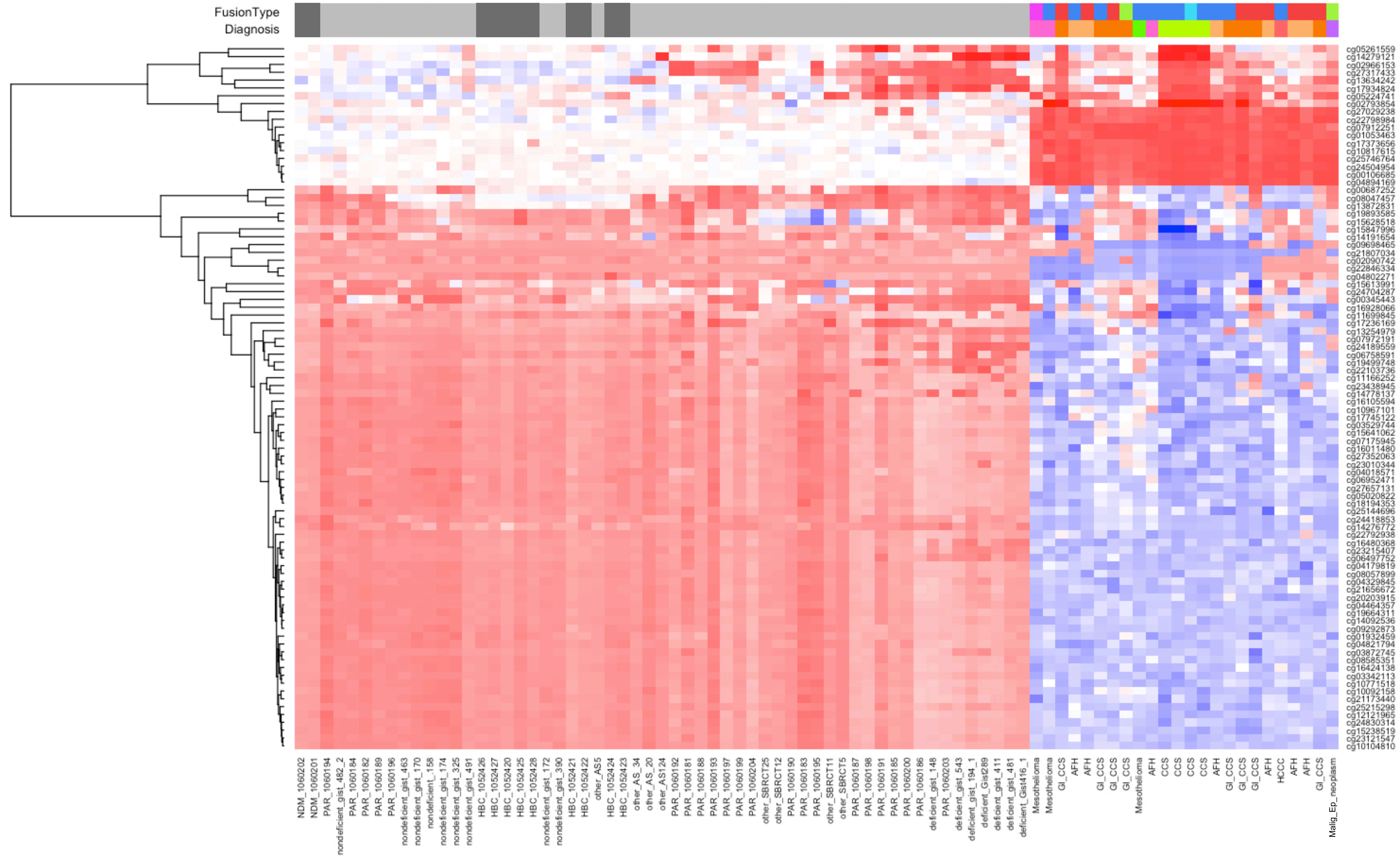
In group: CREB1

No Yes

In group: CREM

No Yes

- Malign_ep_neoplasm
 - Mesothelioma
 - HCCC
 - AFH
 - GI_CCS
 - CCS
 - Normal_tissue
 - Other_soft_tissue_tumors
-
- EWS
 - EWS_ATF1
 - EWS_CREB1
 - EWS_CREM
 - FUS_ATF1



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