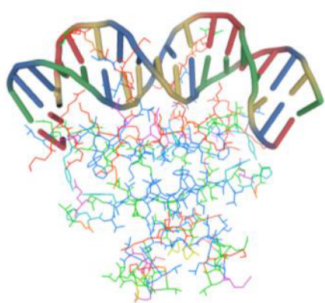


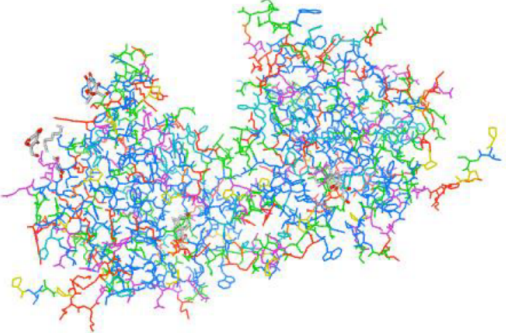
A

>sp|P11831|SRF_HUMAN Serum response factor
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TGGYGPVSGAVS**GAKPGKKT****GRGVKIRMEFIDNKLRRYTFESKKKIGIMKRAYELSLITG**
IQVLLLVASETGHVYTFATRLQPMITSETGKALIQTCNLNSPDSPPRSDPTTDQRMATG
FEETDLTYQVSESDSSGETKDTLKPAFTVTNLPGTTSTIQAPSTSTTMQVSSGSPFIT
NYLAPVSAVSVPASVANGTTLKSTGSGPVSSGGLMQLPSTFTLMPGGAVAQVVPQAI
QVHQAPQASPSRDSSTDLTQTSSTGTVTLPATIMTSSVPTTVGGHMYPSPHAVMYAPT
SGLDGSGLTVLNAFSQAPSTMQVSHSQVQEPGGVPQVFLTASSGTQVIP**VS****AVQLHQ**MAV
IGQAGSSSNLTQLQVNLDTAHSTKSE



B

>sp|Q15596|NCOA2_HUMAN Nuclear receptor coactivator 2
MSGMGENTSDPSRAETRRKKECPDQ**LGSPKPRNTEKRNREQENKYIEELAEILFANFNDI**
DNFNFKPKDKAILKETVKQIRGIKKEQEKAAAAANIDEVQKSDVSSTGQGVIDKDALGPM**IT**
EALDGFFFFVNLGNVVFVSENVTOYLRYNQOELMKNKSVSYLLHVGHDHTEFVKNLLPRSI
VNGGSWSGEPFRRNSHTFNCRLMLVKPLPDSEEEGHNDQEAHQYETMQCFVAVSQPKSIKE
EGEDLQSLCICVARRVPMKERPVLPSSSEFTTRQDLQGGKITSLDSTMTMAAMKPGWEDLV
RRCIQKFHAQHEGESVSYAKRRHHHEVLROGLAFSQIYRFSLSDGTLVAAQTKSKLIRSQT
TNEPQLVISLHMLHREONVCMNPDLTGQTMGKPLNPISNSPAHQALCSGNPGQDMTSL
SNINFPINGPKQMGMPMGRFGSGGMNVHSGMQATTPQGSNYALKMNSPSSQSPGMNPG
QPTSMLSPRHRMSPGVAGSPRIPPSQFSPAGSLHSPVGVCSSTGNSSHYSYTNSSNALQAL
SEGHGVSLSGSSLASPDLMGNLQNSPVNMNPPPLSKMGLSDSKDCFLYGEPESETTGQA
ESSCHPEQGEKTNPNLPPAVSSERADGQSRHLHDSKGQTKLLQLLTCKSDQMEPSPLASS
LSDTNKDSGSLPGSGSTHGTSLKEKHILHRLLDQSSSPVDLAKLTAEATGKDLSDQESS
STAPGSEVTIKQEPVSPKKKENALLRYLLDKDDTKDIGLPEITPKLERLDSKTDPAANTK
LIAMKTEKEEMSEFEPGDQ**PGSELDN**LEEILDDLQNSQLPQLFPDTRPGAPAGSVQKAI
INDLMQLTAENSPTVPVGAQKTALRISQSTFNNRPQGLRLLPNQNLPLDITLQSPGTGAG
PFPPIRNSSPYSVIPPQGMGNQGMIGNQNLGNSSTGMIGNSASRPTMPSGEWAPQSSA
VRVTCATTSAMNRPVQGGMIRNPAASIPMRPSSSQPGQRTLQSQVMNIGPSELEMMNGG
PQYSQQQAPPNQTAWPESILPIDQASFASQNRQPFSSPDDLCPHAAESPDEGALL
DQLYLALRNFDGLEEIDRALGIPELVSQSAVDPEQFSSQSDSNIMLEQKAPVFPQQYASQ
AQMAQGSYSPMQDPNFHTMGQRPSYATLRMQPRPGLRPTGLVQNPQNLRLQLQHLRLQAA
QNRQPLMNQISNVSNVNLTLRPGVPTQAPINAQMLAQQRQREILNQHLRQRQMHQQQQVQ
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PQSPLMSPRMAHTQSPMMQQSQANPAYQAPSDINGWAQNMGGNSMFSQSSPHFGQQAN
TSMYSNNMNIIVSMATNTGMSMGMQMTGQISMTSVTSVPTSGLSSMGPEQVNDPALRG
NLFNPQLPGMDMIKQEGDTRKYC



C

SRF-NCOA2

MLPTQAGAAAAALGRGSALGGSALNRTPTGRPGGGGGTRGANGRRVPGNAGLGPGRLE
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TGGYGPVSGAVS**GAKPGKKT****GRGVKIRMEFIDNKLRRYTFESKKKIGIMKRAYELSLITG**
IQVLLLVASETGHVYTFATRLQPMITSETGKALIQTCNLNSPDSPPRSDPTTDQRMATG
FEETDLTYQVSESDSSGETKDTLKPAFTVTNLPGTTSTIQAPSTSTTMQVSSGSPFIT
NYLAPVSAVSVPASVANGTTLKSTGSGPVSSGGLMQLPSTFTLMPGGAVAQVVPQAI
QVHQAPQASPSRDSSTDLTQTSSTGTVTLPATIMTSSVPTTVGGHMYPSPHAVMYAPT
SGLDGSGLTVLNAFSQAPSTMQVSHSQVQEPGGVPQVFLTASSGTQVIP**VS****AVQLHQPGS**
ELDNLEEILDDLQNSQLPQLFPDTRPGAPAGSVQKAIINDLMQLTAENSPTVPVGAQKT
ALRISQSTFNNRPQGLRLLPNQNLPLDITLQSPGTGAGPFPPIRNSSPYSVIPPQGMGN
NQGMIGNQNLGNSSTGMIGNSASRPTMPSGEWAPQSSAVRVTCATTSAMNRPVQGGMI
RNPAASIPMRPSSSQPGQRTLQSQVMNIGPSELEMMNGGQYQQQAPPNQTAWPESIL
PIDQASFASQNRQPFSSPDDLCPHAAESPDEGALLDQLYLALRNFDGLEEIDRALG
IPELVSQSAVDPEQFSSQSDSNIMLEQKAPVFPQQYASQAQMAQGSYSPMQDPNFHTMGQ
RPSYATLRMQPRPGLRPTGLVQNPQNLRLQLQHLRLQAAQNRQPLMNQISNVSNVNLTLR
PGVPTQAPINAQMLAQQRQREILNQHLRQRQMHQQQQVQRTLMMRGQGLNMTPSMVAPSG
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QANPAYQAPSDINGWAQNMGGNSMFSQSSPHFGQQANTSMYSNNMNIIVSMATNTGGM
SSMNQMTGQISMTSVTSVPTSGLSSMGPEQVNDPALRGGLNLFNPQLPGMDMIKQEGDTR
KYC

Figure S1: FASTA sequences of SRF (A), NCOA2 (B) downloaded from <https://www.uniprot.org/> and the respective three-dimensional structures obtained starting from the FASTA sequences with the use <https://swissmodel.expasy.org/interactive/S4rVBg/models/>. (C) Amino acid sequence of the SRF-NCOA2 fusion protein obtained by joining the two parts of the sequences at the breaking point. The functional domains of each protein were highlighted: MADS-Box (red), DNA-binding (yellow), bHLH-domain (pink), FAS-domain (green), breackpoint (light blue).

Variants by Chromosome

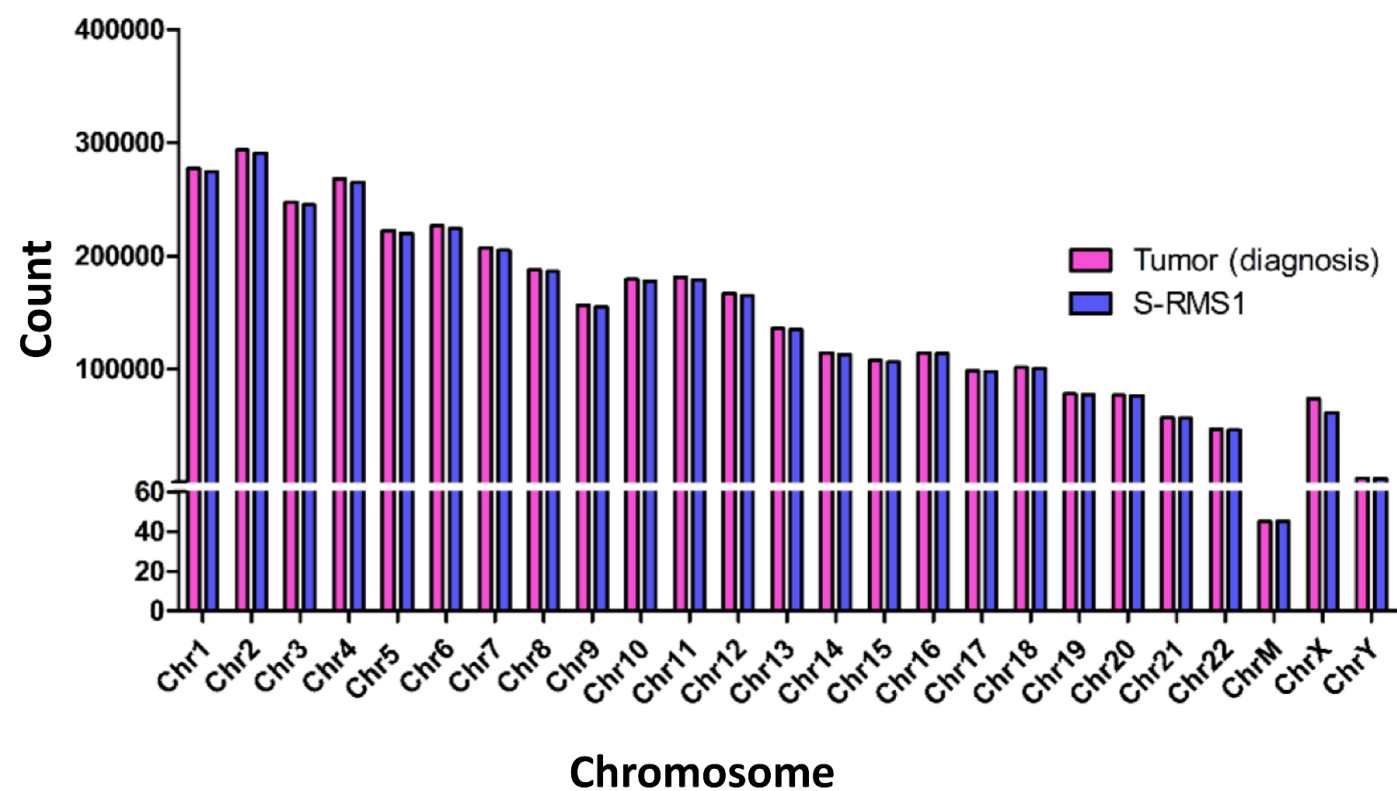


Figure S2: The histogram depicts the number of variant counts in each chromosomes of patient genome for tumor at diagnosis (pink bars) and S-RMS1 (blue bars) samples.

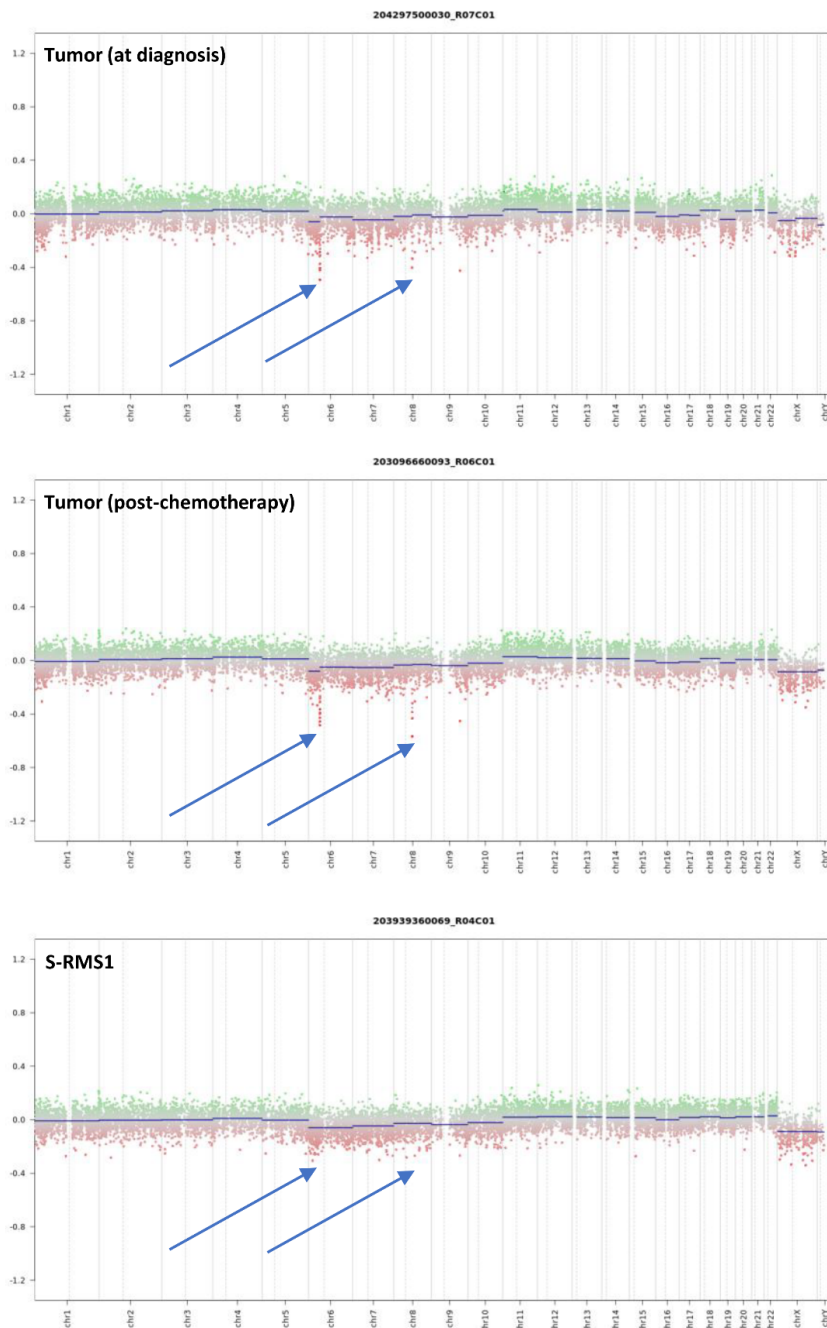
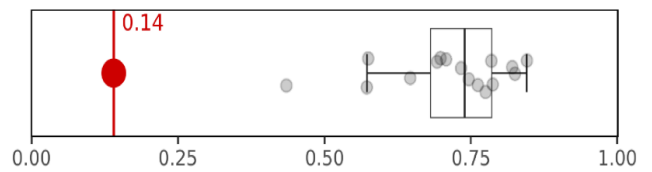
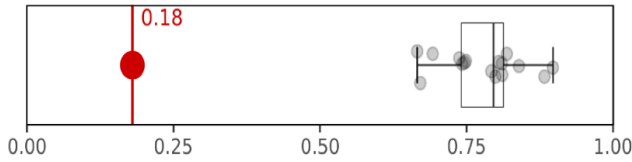


Figure S3: Copy number variation plot calculated from DNA methylation array data of the indicated tumor samples and cell line (S-RMS1). Depiction of structural rearrangements involving autosomes and X/Y chromosomes. Gains/amplifications represent positive (green), losses negative (red) deviations from the baseline. Blue arrows highlight chromosome 6p and 8q deletion corresponding to the breakpoints of SRF and NCOA2 respectively.

Tumor (at diagnosis)

ALMO_MPC

ASPS



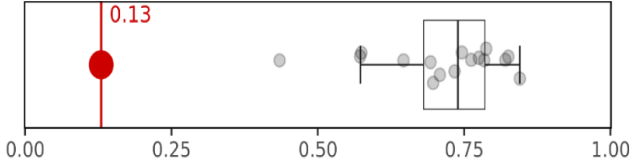
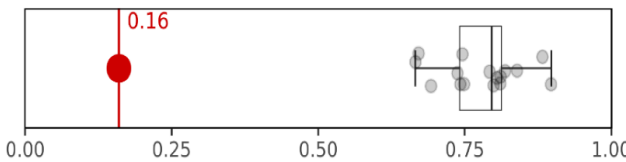
203096660093_R06C01 (red) reference cases (grey)

203096660093_R06C01 (red) reference cases (grey)

Tumor (postchemotherapy)

ALMO_MPC

ASPS



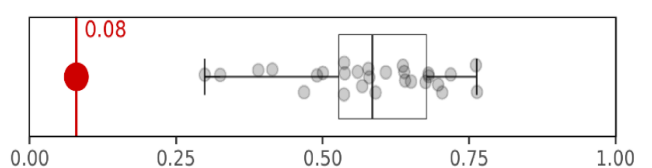
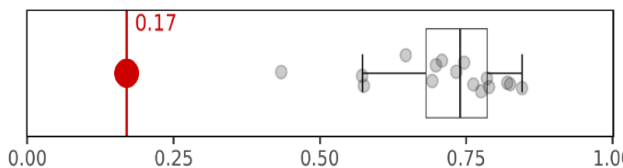
204297500030_R07C01 (red) reference cases (grey)

204297500030_R07C01 (red) reference cases (grey)

S-RMS1

ASPS

RMS_EMB



203939360069_R04C01 (red) reference cases (grey)

203939360069_R04C01 (red) reference cases (grey)

Figure S4: Box-and-whisker plots depicting the first and the second highest raw classification scores (red dot) of the tumor samples and cell line in the indicated methylation classes according to Sarcoma Classifier v12.2 (<https://www.molecularneuropathology.org/mnp/classifier/9>). Grey dots represent the reference cases in the methylation class. ALMO_MPC angioleiomyoma / myopericytoma; ASPS alveolar soft part sarcoma; RMS_EMB rhabdomyosarcoma, embryonal