

Mutational Signatures Vignettes

Single Base Substitution (SBS) Signatures

14 May 2018

Preface

As the number of mutational signatures has increased it has become increasingly difficult to keep in mind their mutational features, aetiology, and other attributes. We have therefore written a "vignette" for each mutational signature. The vignettes include mutational profiles and notes on potential aetiology, associated mutational signatures, how the signature has changed during iterations of analysis and other pertinent comments. These are intended to be short, very high level, "aides-memoire" for key elements of what we know, suspect or has been widely discussed for each signature. They are not intended to be comprehensive summaries of everything reported in the scientific literature and they are not referenced.

Figure legends

Many of the vignettes have four figures.

Within each vignette:

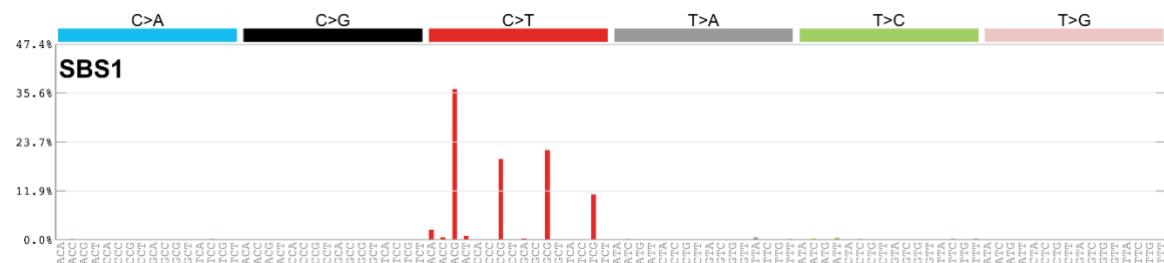
The first figure (eg SBS1) shows the signature profile using the 96 mutation type classification and the same conventions as Figure 2 in the main text.

The second figure (eg SBS1-TSB) shows the signature profile on transcribed and untranscribed strands of genes using the 192 mutation type classification.

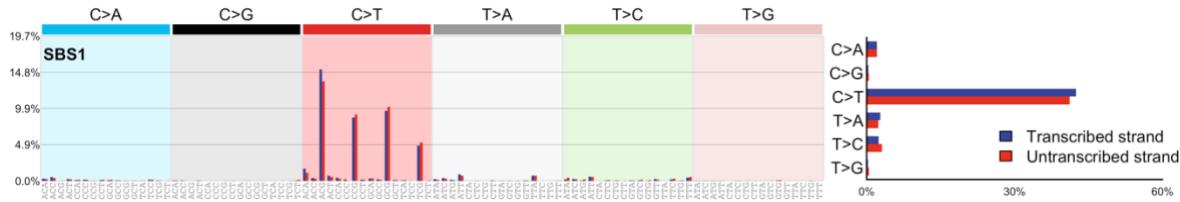
The third figure, "Cancer types in which the signature is found," shows the numbers of mutations per megabase attributed to each mutational signature in samples with the signature. Only those cancer types with tumors in which signature activity is attributed are shown. The numbers below the dots for each cancer type indicate the number of tumors in which the signature was attributed (above the blue horizontal bar) and the total number of tumors analyzed (below the blue bar).

The fourth figure, "Differences between current and previous profiles," is only shown for signatures for which there has been a similar figure previously shown in COSMIC.

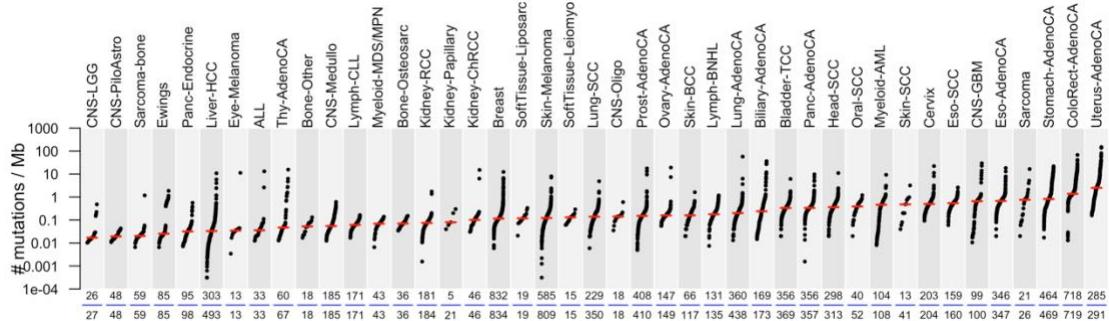
SBS1 (v3.0)



SBS1-TSB



Cancer types in which the signature is found



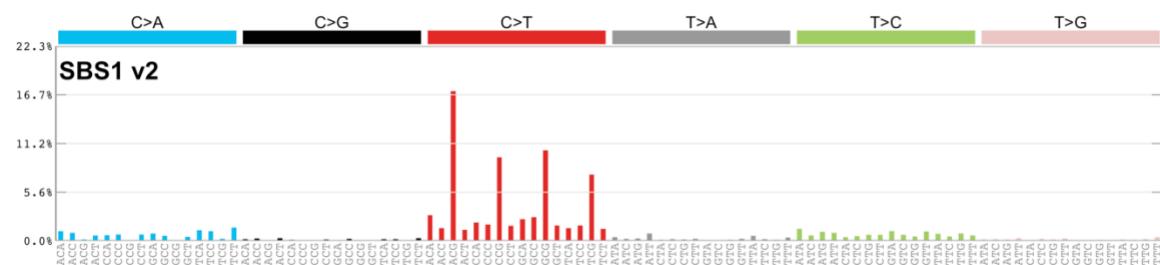
Proposed aetiology

An endogenous mutational process initiated by spontaneous or enzymatic deamination of 5-methylcytosine to thymine which generates G:T mismatches in double stranded DNA. Failure to detect and remove these mismatches prior to DNA replication results in fixation of the T substitution for C.

Associated mutation classes and signatures

The activity of SBS1 is closely correlated with the activity of SBS5 within many types of cancer. However, between cancer types, mutation burdens of SBS1 and SBS5 do not clearly correlate consistent with them being due to different underlying processes.

Differences between current and previous signatures

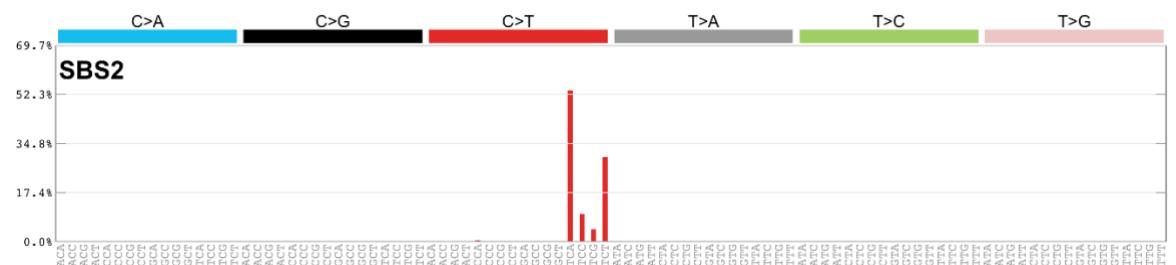


The contribution of C>T mutations not at NCG trinucleotides and of mutations other than C>T has diminished markedly compared to previous versions which were likely more contaminated by Signature SBS5 and other signatures. The cosine similarity between the prior and current versions of signature SBS1 is 0.95.

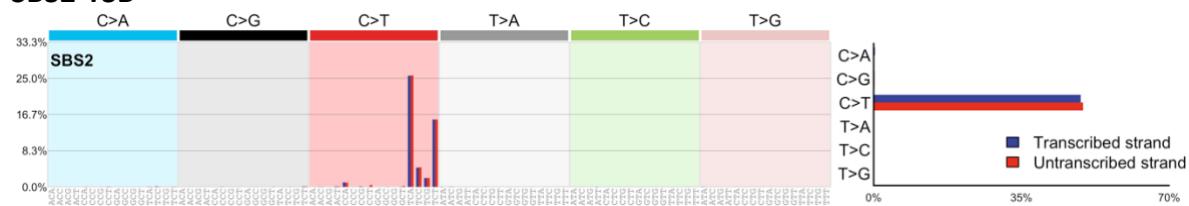
Comments

Signature SBS1 is clock-like in that the number of mutations in most cancers and normal cells correlates with the age of the individual. Rates of acquisition of Signature SBS1 mutations over time differ markedly between different cancer types and different normal cell types. These differences correlate with estimated rates of stem cell division in different tissues and Signature SBS1 may therefore be a cell division/mitotic clock.

SBS2 (v3.0)



SBS2-TSB

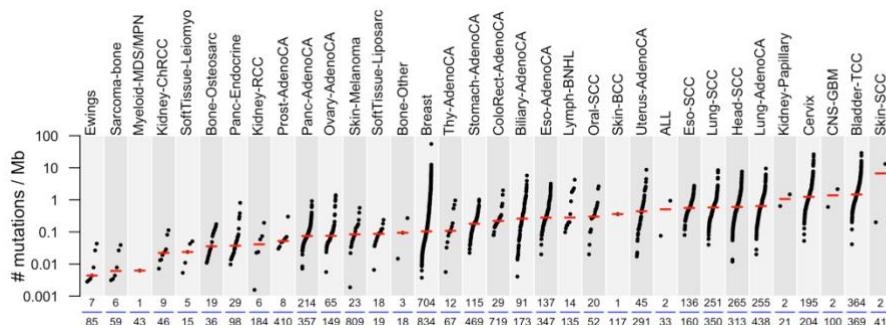


SBS2-TSB in exons



Although the plot shows no obvious transcriptional strand bias over the whole transcribed genome, there appears to be transcriptional strand bias in exons which is therefore not present or is much weaker in introns.

Cancer types in which the signature is found



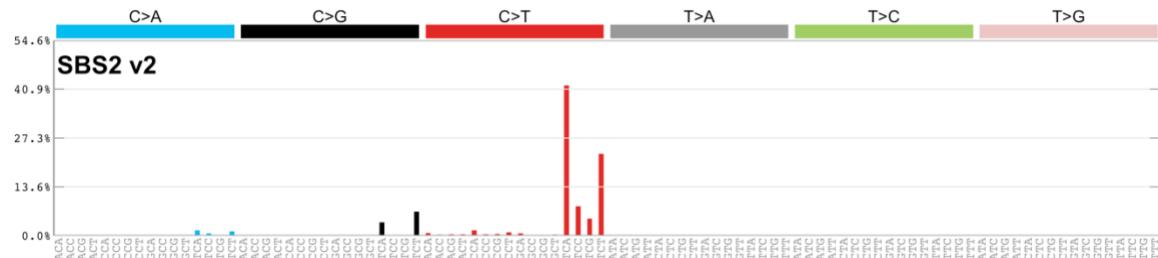
Proposed aetiology

Attributed to activity of the AID/APOBEC family of cytidine deaminases on the basis of similarities in the sequence context of cytosine mutations caused by APOBEC enzymes in experimental systems. APOBEC3A is probably responsible for most mutations in human cancer, although APOBEC3B may also contribute (these differ in the sequence context two bases 5' to the mutated cytosine, see 1,536 mutation classification signature extraction). SBS2 mutations may be generated directly by DNA replication across uracil or by error prone polymerases replicating across abasic sites generated by base excision repair removal of uracil.

Associated mutation classes and signatures

SBS2 is closely associated with SBS13. SSBS2 is also associated with DBS11, which is characterised predominantly by CC>TT doublet base substitutions as well as other CC>NN doublet base substitutions.

Differences between current and previous profiles

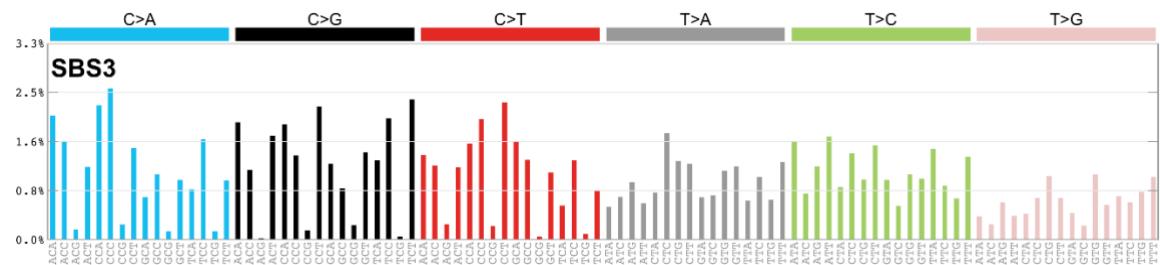


The contributions of C>G and C>A mutations at T_{CN} trinucleotides have diminished compared to previous profiles indicating reduced contamination by SBS13. The cosine similarity between the prior and current versions of SBS2 is 0.99.

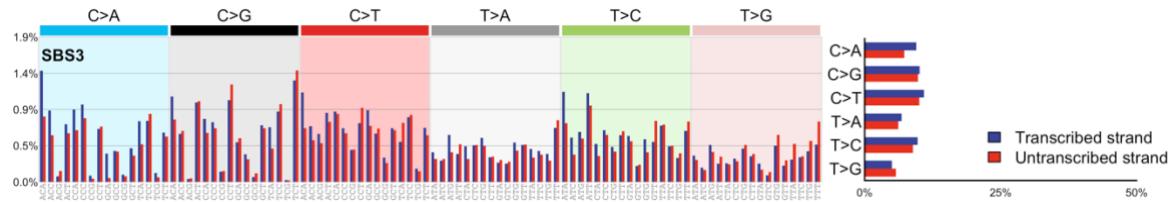
Comments

SBS2 is usually found in the same samples as SBS13. It has been proposed that activation of AID/APOBEC cytidine deaminases in cancer may be due to previous viral infection, retrotransposon jumping, or tissue inflammation. Currently, there is limited evidence to support these hypotheses. Germline polymorphisms involving APOBEC3A and APOBEC3B are associated with predisposition to breast and bladder cancer as well as with mutation burdens of SBS2 and SBS13. Mutations of similar patterns to SBS2 and SBS13 are commonly found in the phenomenon of local hypermutation present in some cancers, known as kataegis, implicating AID/APOBEC enzymes in this process as well.

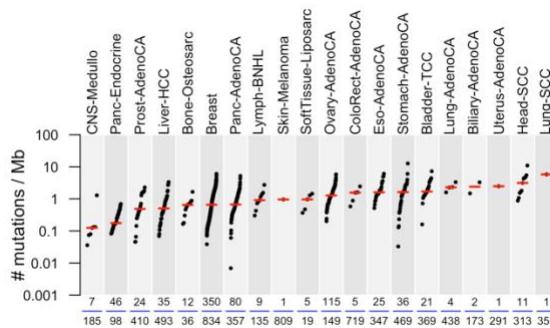
SBS3 (v3.0)



SBS3-TSB



Cancer types in which the signature is found



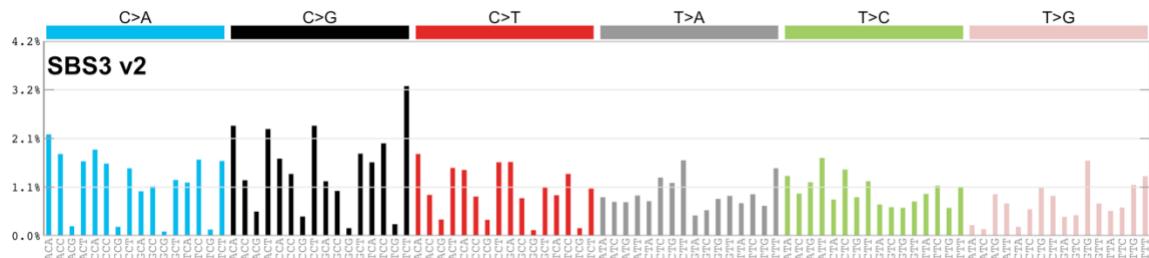
Proposed aetiology

Defective homologous recombination-based DNA damage repair which manifests predominantly as small indels and genome rearrangements due to abnormal double strand break repair but also in the form of this base substitution signature.

Associated mutation classes and signatures

Associated with ID6, characterised by small deletions of >5bp with extended stretches of overlapping microhomology at breakpoint junctions. Also associated with multiple genome rearrangement mutational signatures; short tandem duplications (1-10kb); longer tandem duplications (>100kb); deletions (1-10kb).

Differences between current and previous profiles

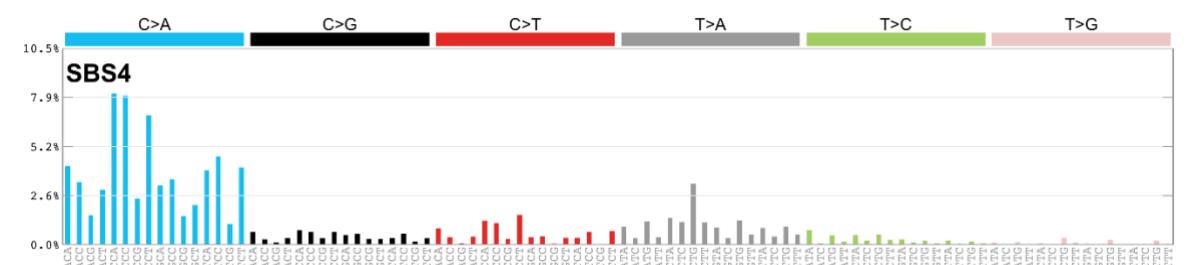


The cosine similarity between the prior and current versions of SBS3 is 0.96.

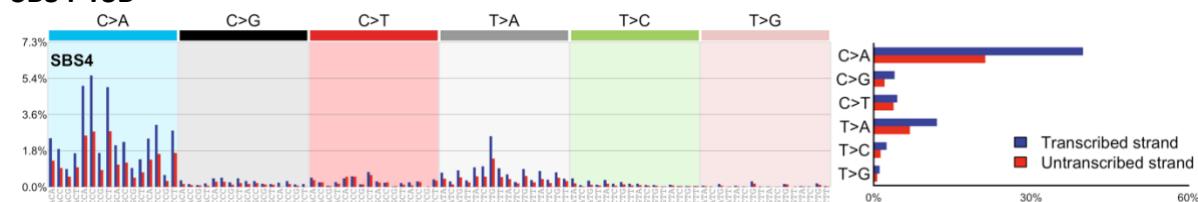
Comments

SBS3 is strongly associated with germline and somatic *BRCA1* and *BRCA2* mutations and *BRCA1* promoter methylation in breast, pancreatic, and ovarian cancers. In pancreatic cancer, responders to platinum therapy usually exhibit SBS3 mutations. Together with associated indel and rearrangement signatures, SBS3 has been proposed as a predictor of defective homologous recombination-based repair and thus of response to therapies exploiting this repair defect.

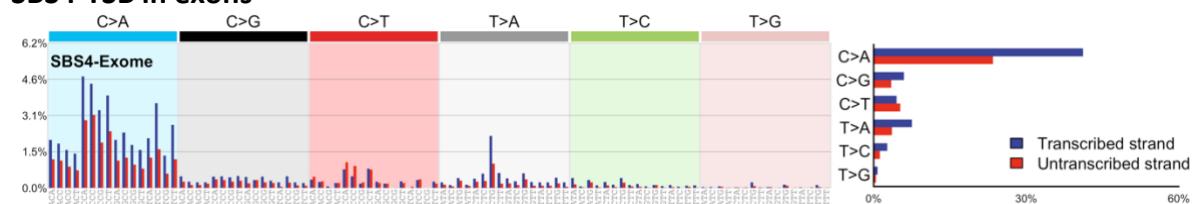
SBS4 (v3.0)



SBS4-TSB

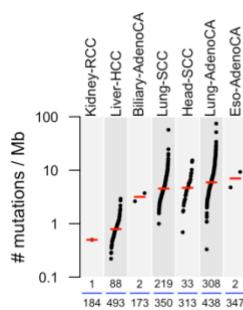


SBS4-TSB in exons



SBS4 exhibits transcriptional strand bias for C>A (and also T>A mutations) with more mutated G than C bases on the untranscribed strands of genes consistent with damage to guanine and activity of transcription-coupled nucleotide excision repair. The transcriptional strand bias also exists in exonic regions.

Cancer types in which the signature is found



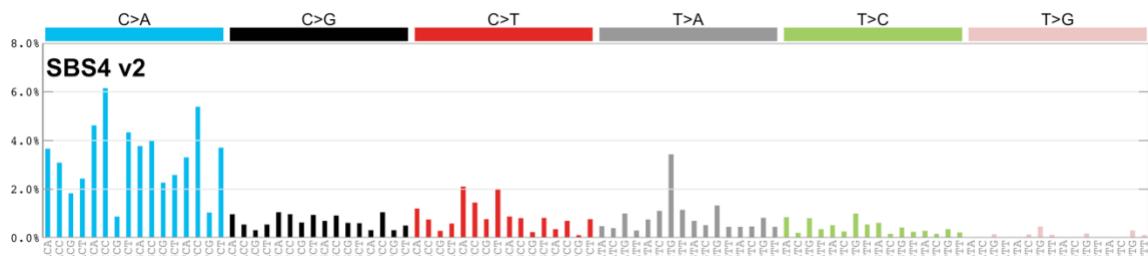
Proposed aetiology

Associated with tobacco smoking. Its profile is similar to the mutational spectrum observed in experimental systems exposed to tobacco carcinogens such as benzo[a]pyrene. SBS4 is, therefore, likely due to direct DNA damage by tobacco smoke mutagens.

Associated mutation classes and signatures

Associated with ID3, characterised by single base deletions of predominantly C, and with DBS2, characterised predominantly by CC>AA mutations.

Differences between current and previous profiles

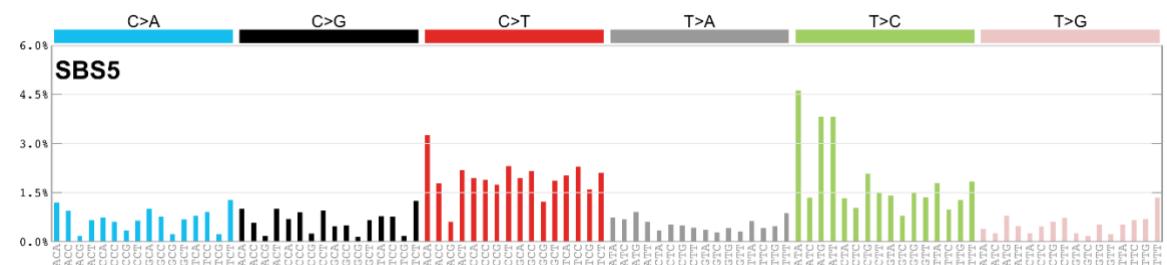


The cosine similarity between the prior and current versions of signature SBS4 is 0.94.

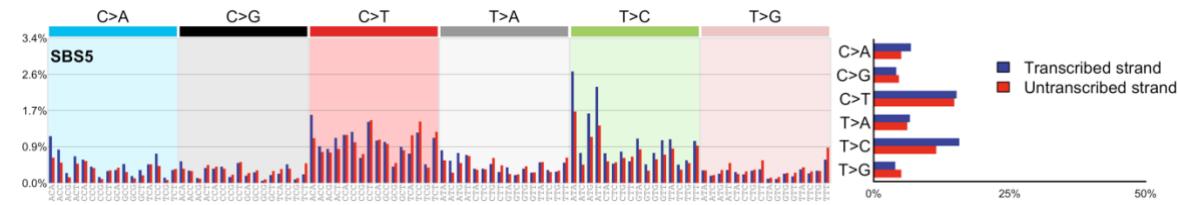
Comments

Although tobacco smoking causes multiple cancer types in addition to lung and head and neck, SBS4 has not been detected in many of these. SBS29 is found in cancers associated with tobacco chewing and appears different from SBS4.

SBS5 (v3.0)

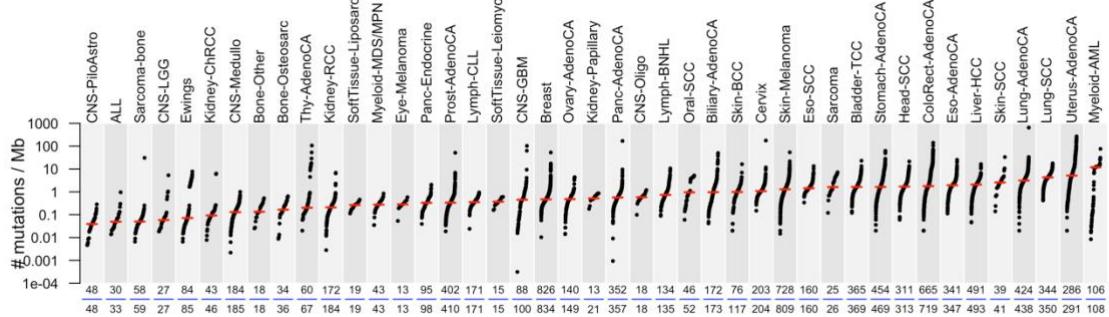


SBS5-TSB



Transcriptional strand bias for T>C substitutions at ATN context with more mutated A than T bases on the untranscribed strands of genes compatible with damage to adenine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



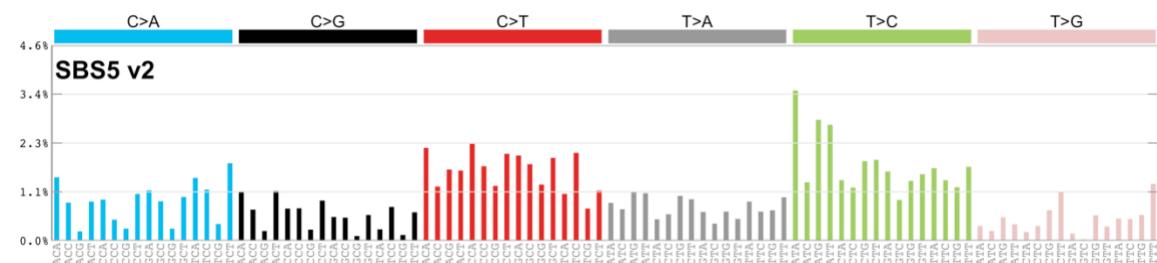
Proposed aetiology

Unknown. SBS5 mutational burden is increased in bladder cancer samples with ERCC2 mutations and in many cancer types due to tobacco smoking.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

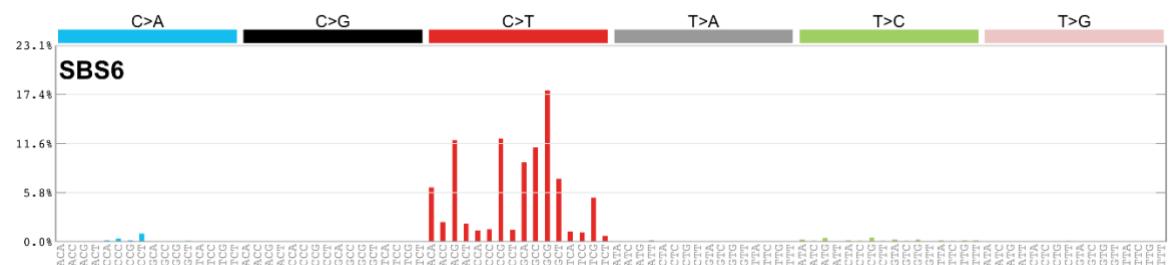


The profile of SBS5 exhibits less contamination by SBS1. The cosine similarity between the prior and current versions of SBS5 is 0.96.

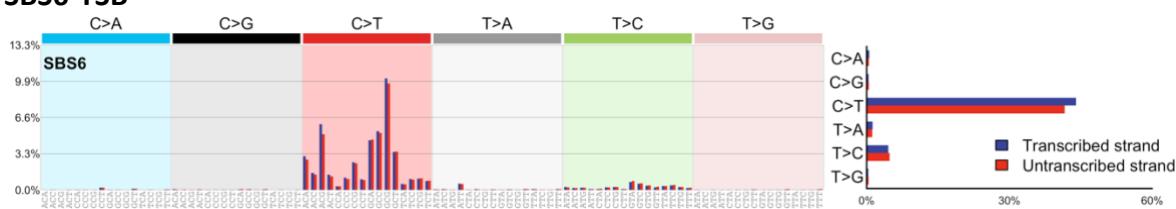
Comments

SBS5 is clock-like in that the number of mutations in most cancers and normal cells correlates with the age of the individual. Rates of acquisition of SBS5 mutations over time differ between different cancer types and different normal cell types. These differences do not clearly correlate with estimated rates of stem cell division in different tissues nor with differences in SBS1 mutation rates. SBS5 may be contaminated by SBS16.

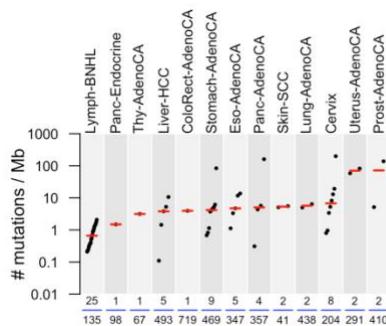
SBS6 (v3.0)



SBS6-TSB



Cancer types in which the signature is found



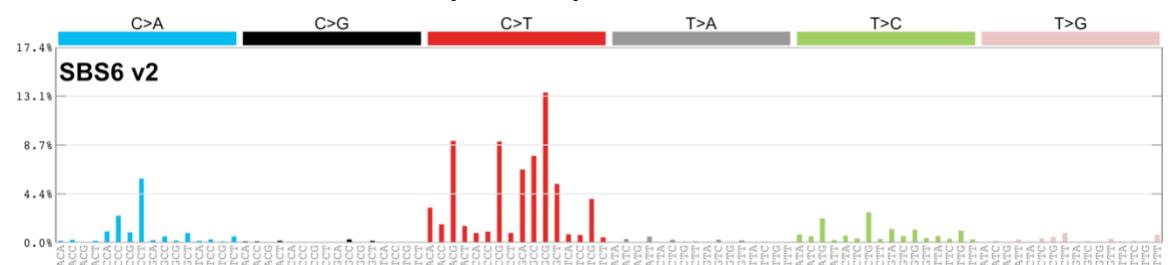
Proposed aetiology

SBS6 is associated with defective DNA mismatch repair and is found in microsatellite unstable tumours.

Associated mutation classes and signatures

SBS6 is associated with large numbers of ID1 and ID2 mutations, which are characterised respectively by small (usually 1bp) insertions and deletions of T at mononucleotide T repeats.

Differences between current and previous profiles

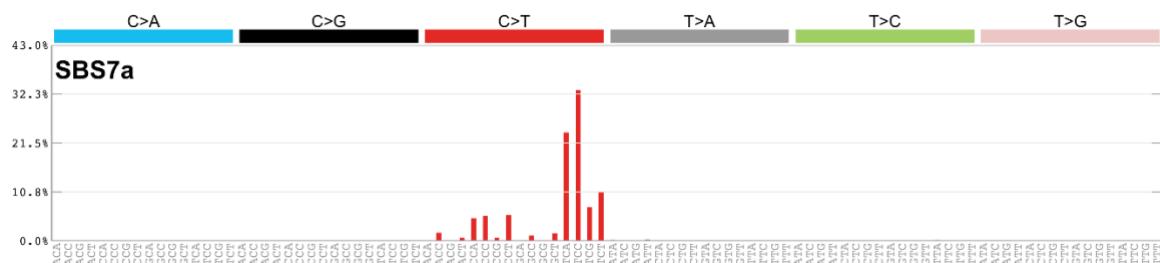


The profile of SBS6 exhibits less contamination by other DNA mismatch repair deficiency signatures. The cosine similarity between the prior and current versions of SBS6 is 0.95.

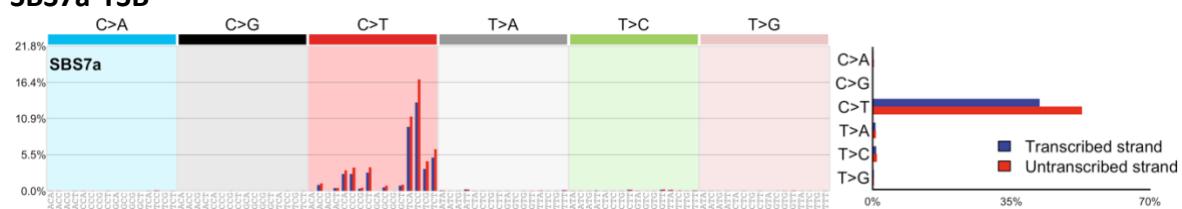
Comments

SBS6 is one of seven mutational signatures associated with defective DNA mismatch repair (with microsatellite instability, MSI) and is often found in the same samples as other MSI associated signatures: SBS14, SBS15, SBS20, SBS21, SBS26, and SBS44.

SBS7a (v3.0)

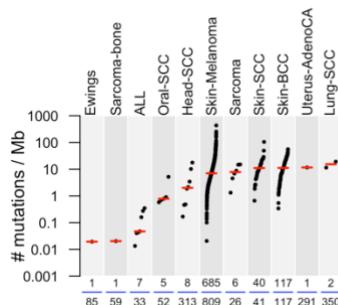


SBS7a-TSB



Transcriptional strand bias with more mutated C than G bases on untranscribed strands of genes compatible with damage to cytosine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



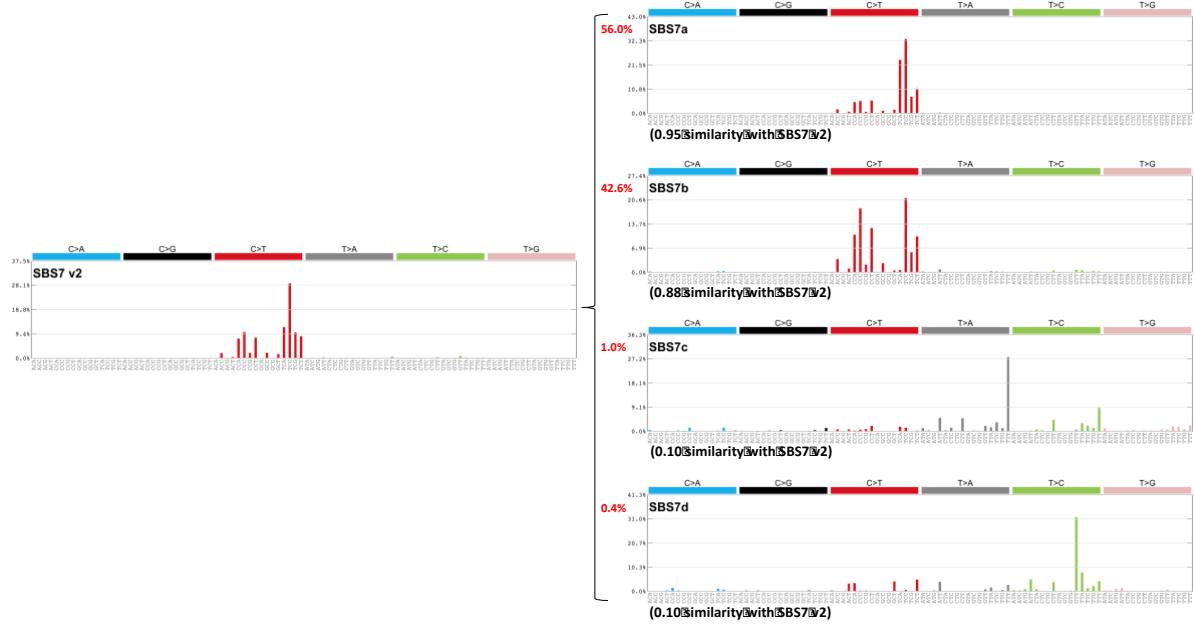
Proposed aetiology

SBS7a/b/c/d are found in cancers of the skin from sun exposed areas and are thus likely to be due to exposure to ultraviolet light. SBS7a may possibly be the consequence of just one of the two major known UV photoproducts, cyclobutane pyrimidine dimers or 6-4 photoproducts. However, there is currently no evidence for this hypothesis and it is unclear which of these photoproducts may be responsible for SBS7a.

Associated mutation classes and signatures

SBS7a is associated with SBS7b/c/d and these signatures are commonly found in the same samples. SBS7a is associated with DBS1, which exhibits predominantly CC>TT mutations and with ID13, which is predominantly characterised by single base T deletions at TT dinucleotides.

Differences between current and previous profiles

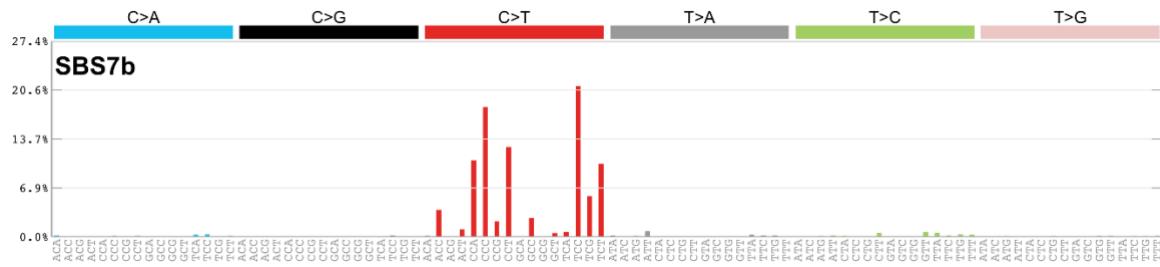


The much larger number of melanoma whole genome sequences now analysed allows splitting of SBS7 into four distinct components, termed SBS7a/b/c/d, that together recapitulate the prior pattern of SBS7.

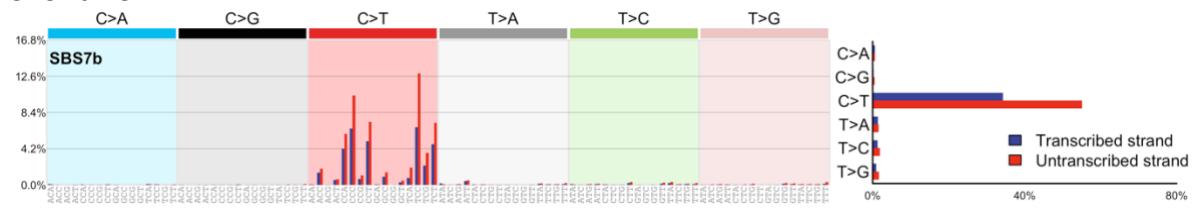
Comments

N/A

SBS7b (v3.0)

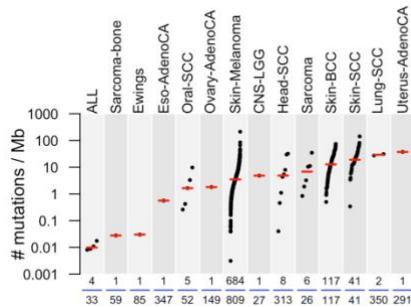


SBS7b-TSB



Transcriptional strand bias with more mutated C than G bases on untranscribed strands of genes compatible with damage to cytosine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



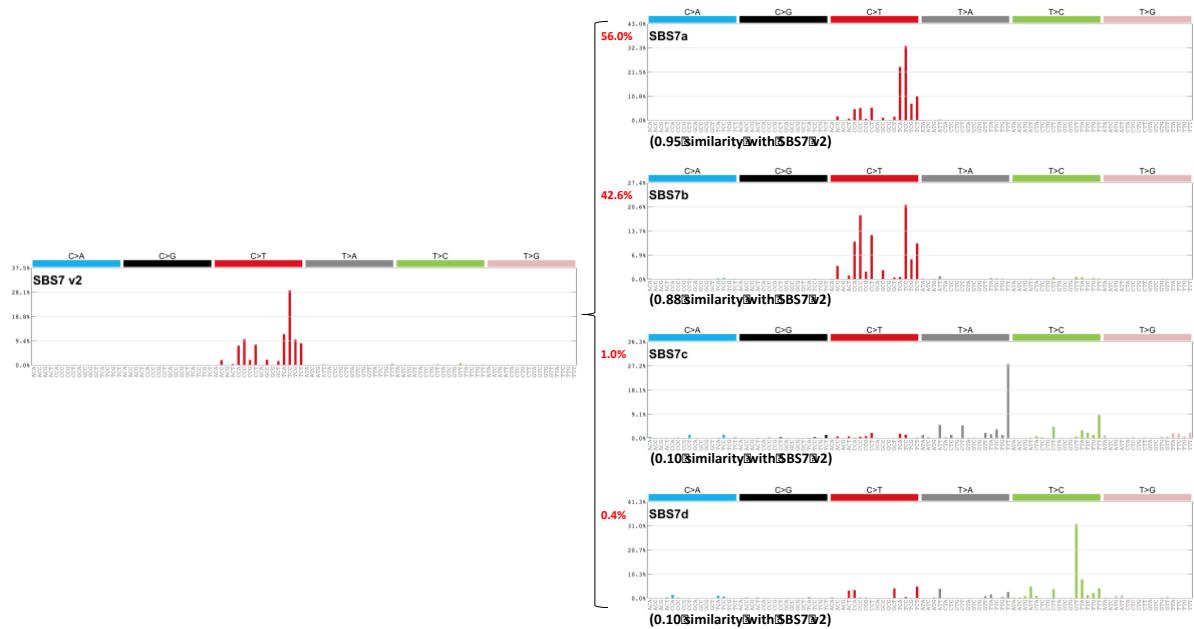
Proposed aetiology

SBS7a/b/c/d are found in cancers of the skin from sun exposed areas and are likely to be due to exposure to ultraviolet light. SBS7b may possibly be the consequence of just one of the two major known UV photoproducts, cyclobutane pyrimidine dimers or 6-4 photoproducts. However, there is no evidence for this hypothesis and it is unclear which of these photoproducts may be responsible for SBS7b.

Associated mutation classes and signatures

SBS7b is associated with SBS7a/c/d and these signatures are commonly found in the same samples. SBS7b is associated with DBS1, which exhibits predominantly CC>TT mutations and also with ID13, which is predominantly characterised by T deletions at TT dinucleotides.

Differences between current and previous profiles

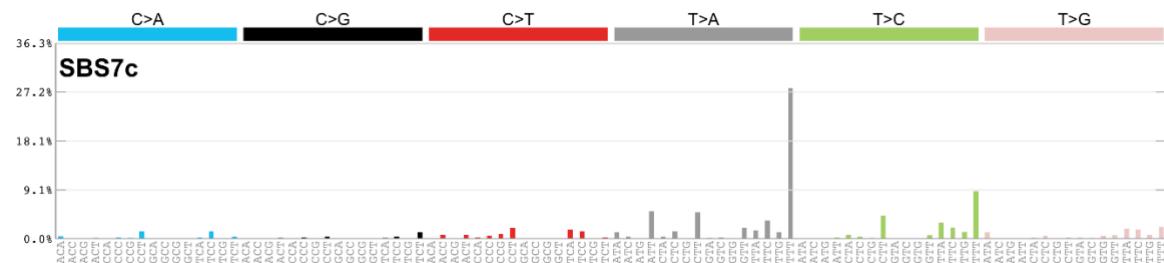


The larger number of analysed samples allows splitting of SBS7 into four distinct components, termed SBS7a/b/c/d, that together recapitulate the prior pattern of SBS7.

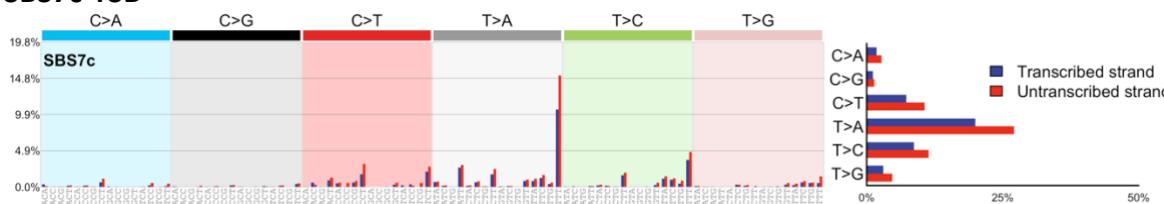
Comments

N/A

SBS7c (v3.0)

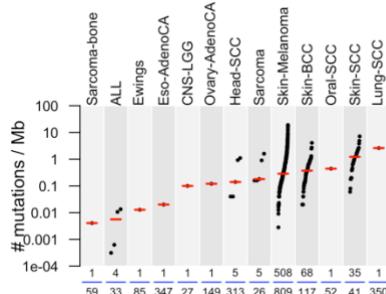


SBS7c-TSB



Transcriptional strand bias with more mutated T than A bases on untranscribed strands compatible with damage to thymidine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



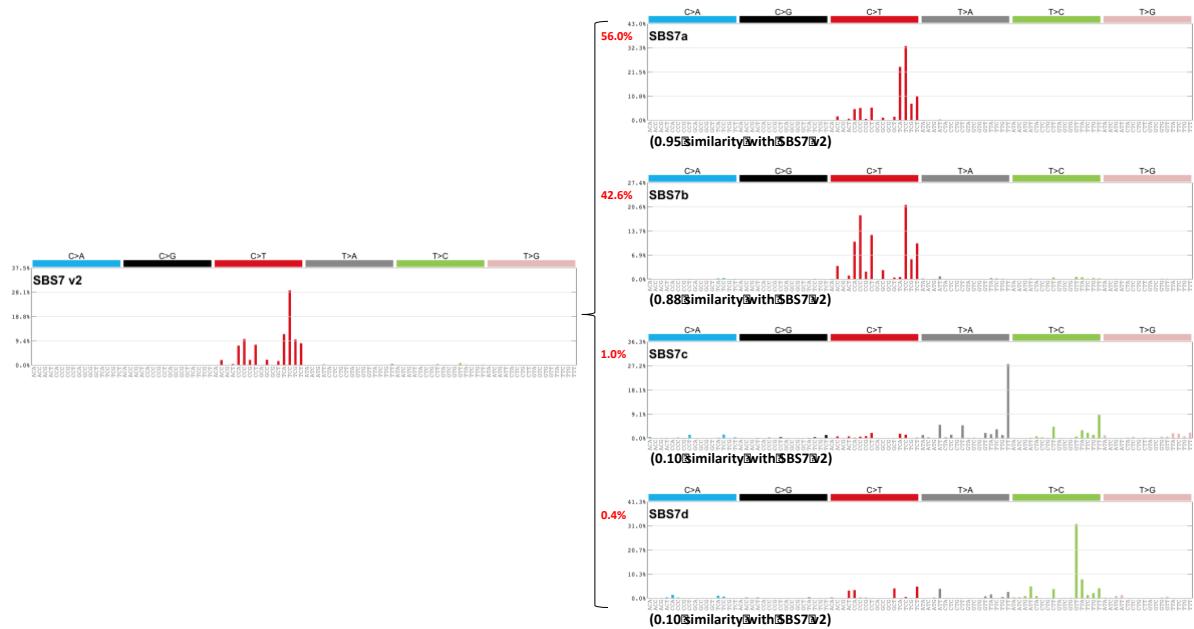
Proposed aetiology

SBS7a/b/c/d are found in cancers of the skin from sun exposed areas and are likely to be due to exposure to ultraviolet light. SBS7c is possibly the consequence of translesion DNA synthesis by enzymes with propensity to insert T, rather than A, opposite ultraviolet induced thymidine and cytidine photodimers. The preponderance of T>A rather than T>C mutations may reflect the heavier burden of thymidine compared to cytidine dimers induced by UV light.

Associated mutation classes and signatures

SBS7c is associated with SBS7a/b/d and these signatures are commonly found in the same samples.

Differences between current and previous profiles

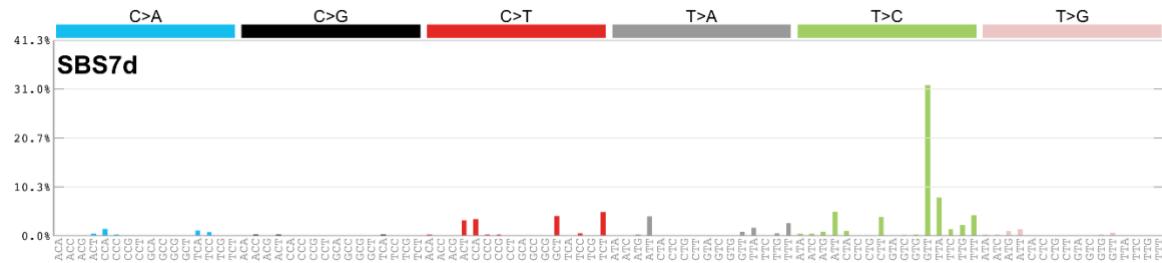


The larger number of whole genome samples now analysed allows splitting of SBS7 into four distinct components, termed SBS7a/b/c/d, that together recapitulate the prior pattern SBS7.

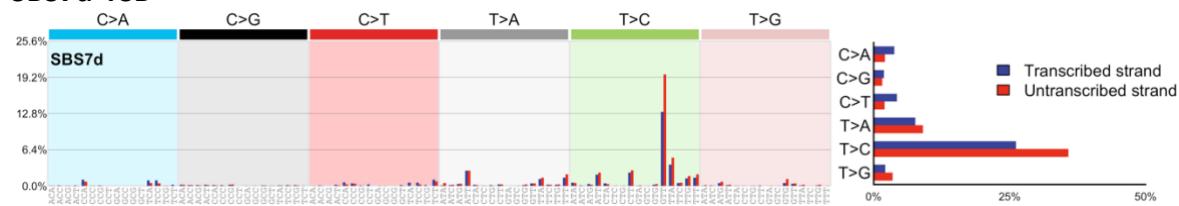
Comments

N/A

SBS7d (v3.0)

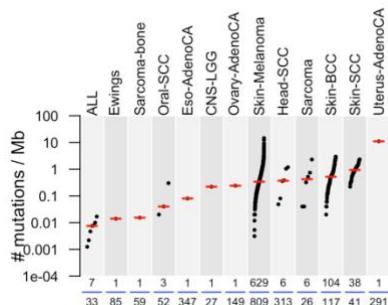


SBS7d-TSB



Transcriptional strand bias with more mutated T than A on untranscribed strands of genes compatible with damage to thymidine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



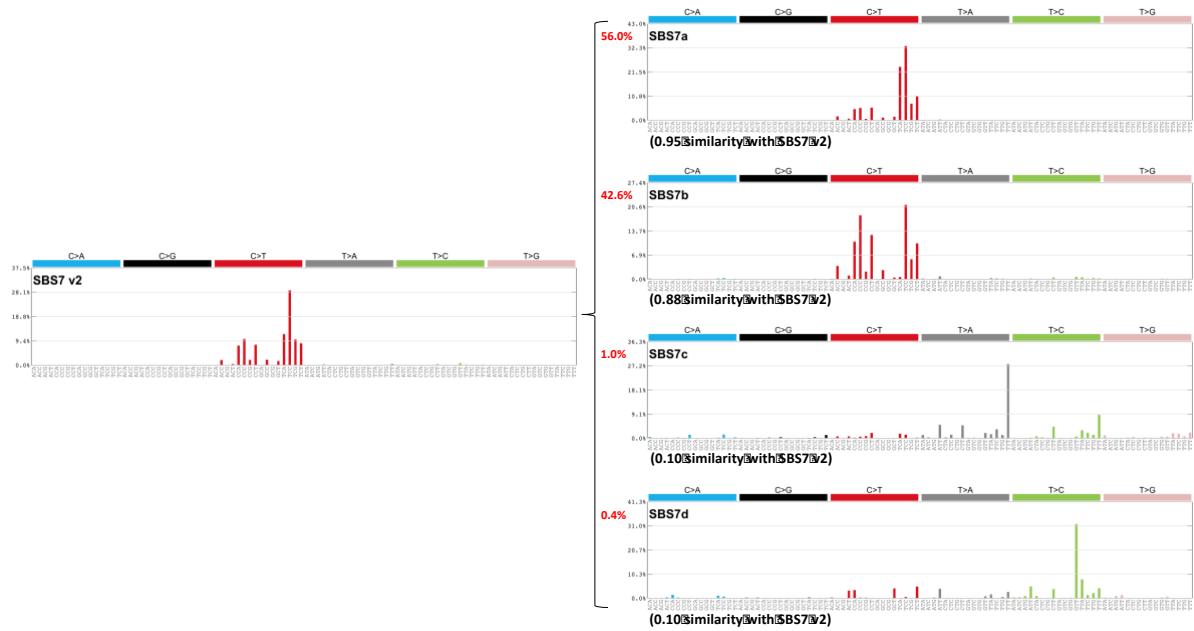
Proposed aetiology

SBS7a/b/c/d are found in cancers of the skin from sun exposed areas and are likely to be due to exposure to ultraviolet light. SBS7d is possibly the consequence of translesion DNA synthesis by error-prone polymerases with greater propensity to insert G, rather than A, opposite UV light induced thymidine and cytidine photodimers.

Associated mutation classes and signatures

SBS7d is associated with SBS7a/b/c and these signatures are commonly found in the same samples.

Differences between current and previous profiles

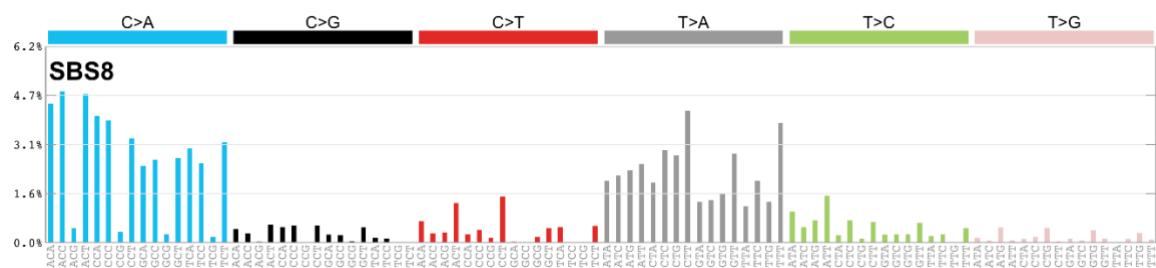


The larger number of whole genome sequenced samples allows splitting of SBS7 into four distinct components, termed SBS7a/b/c/d that together recapitulate the prior pattern of SBS7.

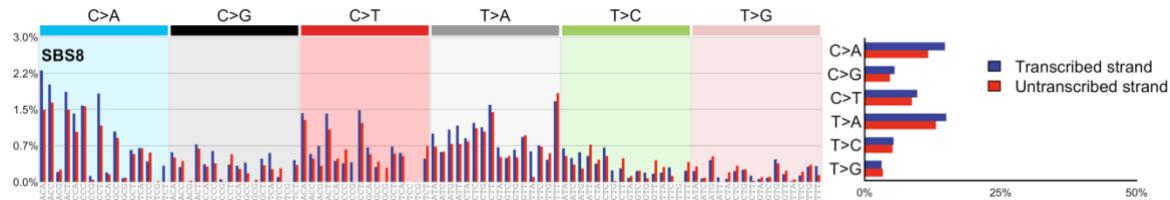
Comments

N/A

SBS8 (v3.0)

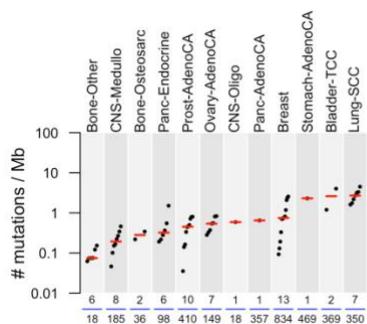


SBS8-TSB



Transcriptional strand bias for C>A substitutions with more mutated G than C on the untranscribed strand, compatible with damage to guanine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



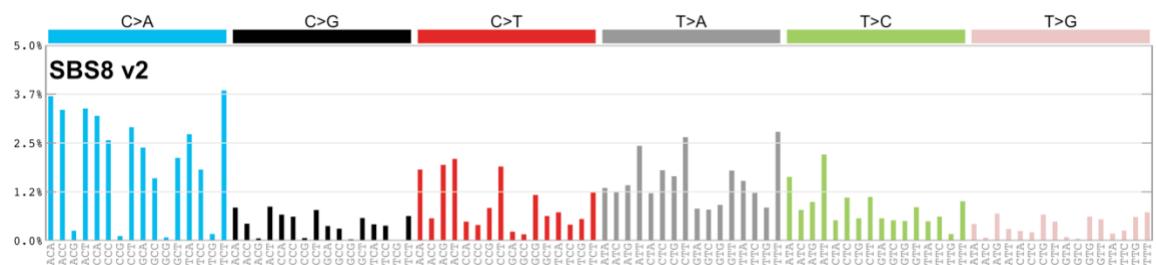
Proposed aetiology

Unknown.

Associated mutation classes and signatures

SBS8 is associated with CC>AA mutations.

Differences between current and previous profiles

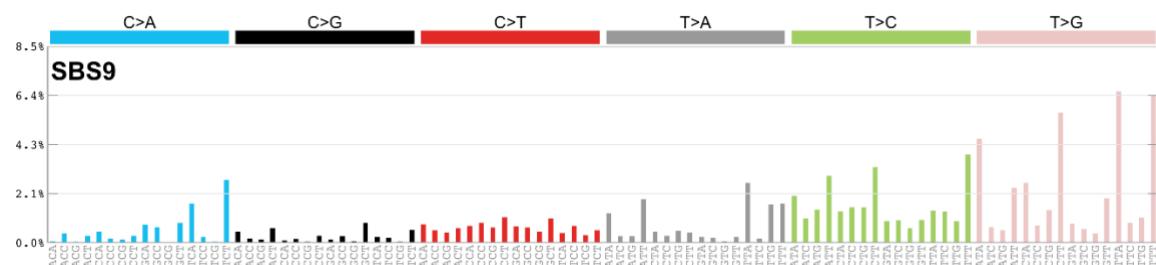


The pattern of SBS8 exhibits smaller contributions of C>T and T>C mutations, possibly reflecting greater separation between signatures SBS3 and SBS8. The cosine similarity between the prior and current versions of signature SBS8 is 0.94.

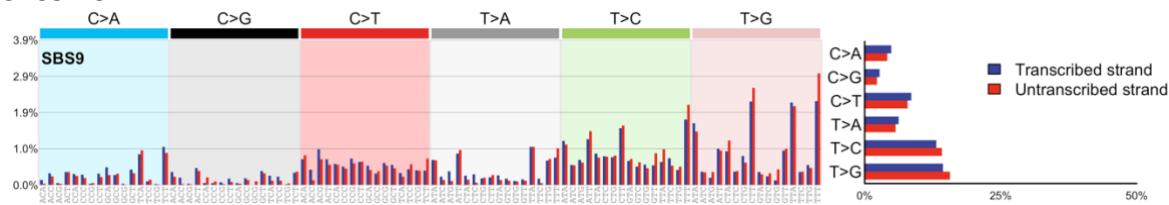
Comments

N/A

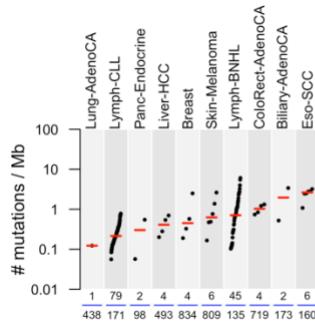
SBS9 (v3.0)



SBS9-TSB



Cancer types in which the signature is found



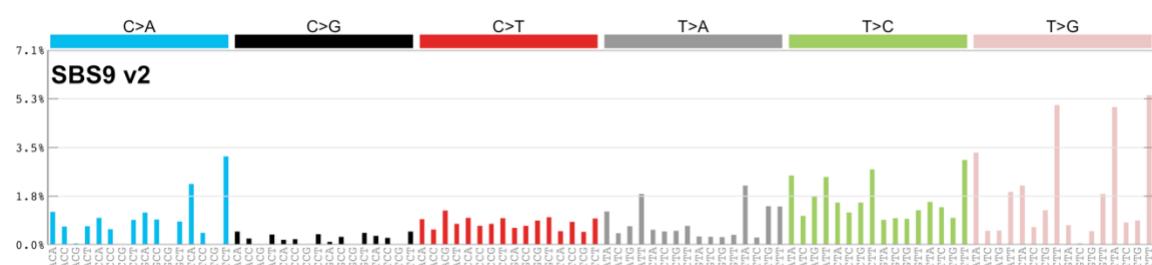
Proposed aetiology

Attributed to mutations induced during replication by polymerase eta as part of somatic hypermutation in lymphoid cells.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

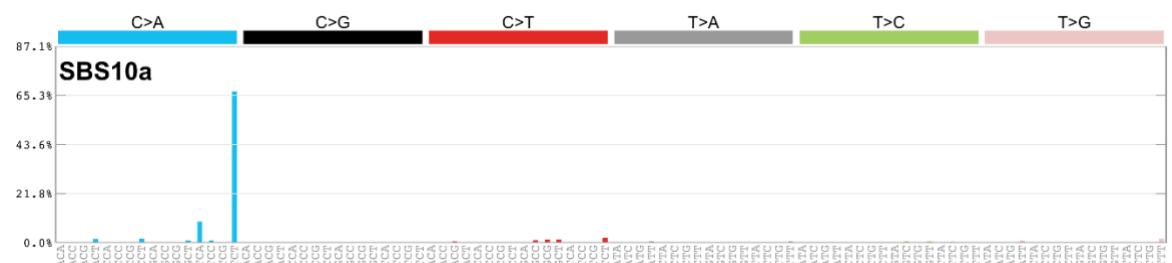


The pattern of SBS9 has been quite stable. The cosine similarity between the prior and current versions of signature SBS9 is 0.98.

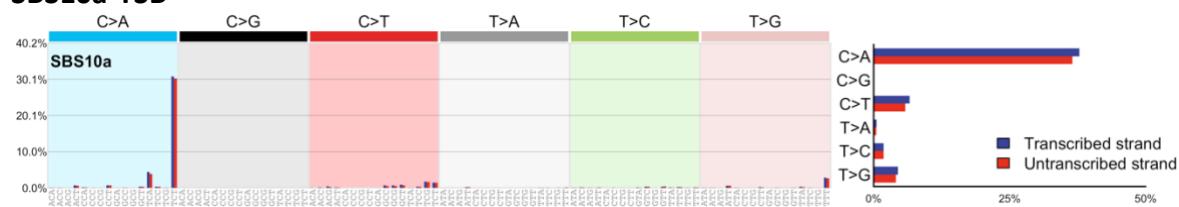
Comments

Chronic lymphocytic leukaemias that possess immunoglobulin gene hypermutation (IGHV-mutated) have elevated numbers of mutations attributed to SBS9 compared to those that do not have immunoglobulin gene hypermutation.

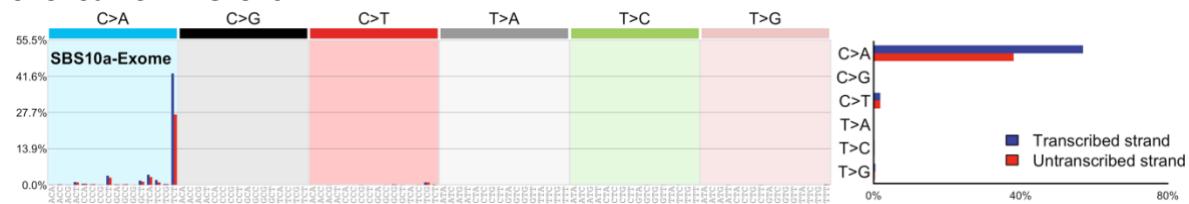
SBS10a (v3.0)



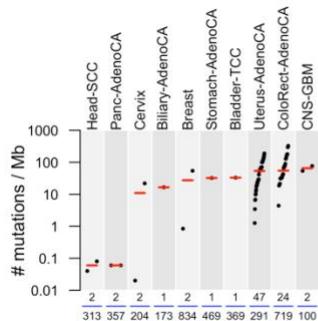
SBS10a-TSB



SBS10a-TSB in exons



Cancer types in which the signature is found



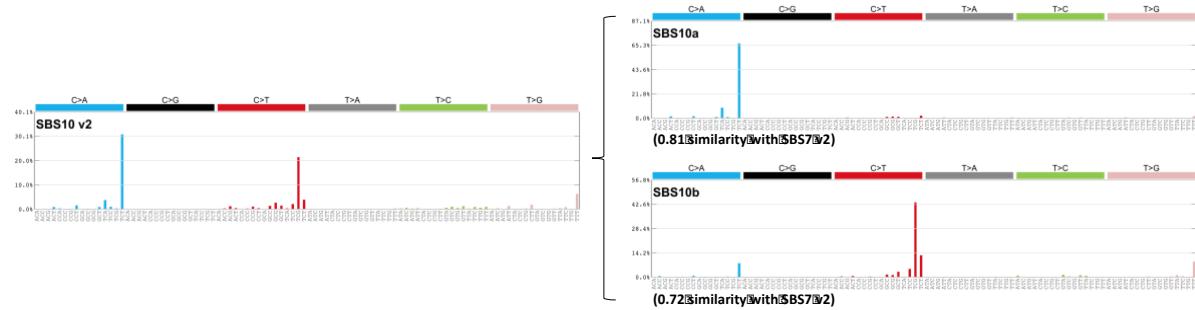
Proposed aetiology

Polymerase epsilon exonuclease domain mutations.

Associated mutation classes and signatures

SBS10a is associated with SBS10b and SBS28 and these signatures are commonly found in the same samples. DBS3 is also associated with SBS10a/b.

Differences between current and previous profiles

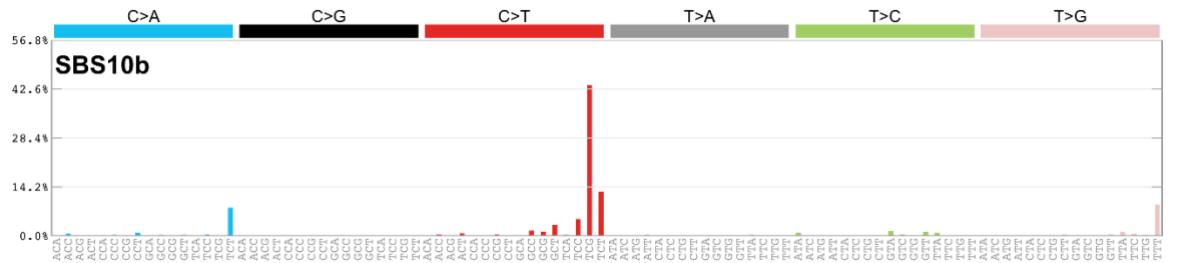


The larger number of analysed samples allows splitting of SBS10 into two distinct components, termed SBS10a/b. SBS28 is also found in most samples with SBS10a/b potentially accounting for the T>G component of the previous SBS10.

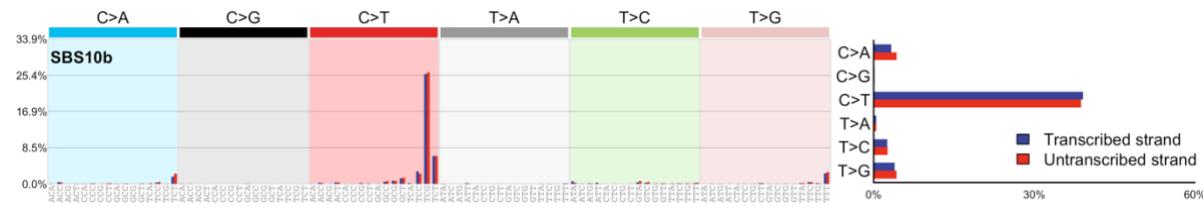
Comments

SBS10a/b usually generate large numbers of somatic mutations (>100 mutations per MB) and samples with these signatures have been termed hypermutators.

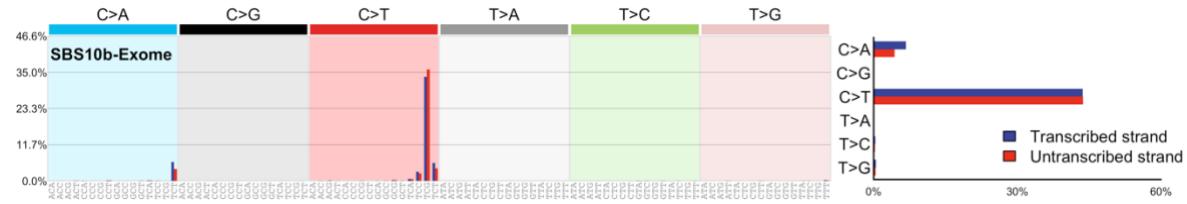
SBS10b (v3.0)



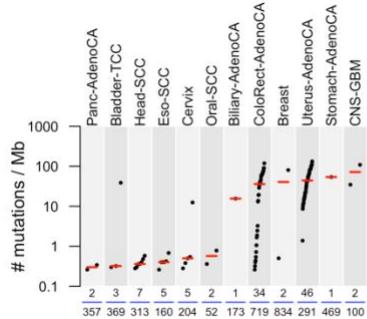
SBS10b-TSB



SBS10b-TSB in exons



Cancer types in which the signature is found



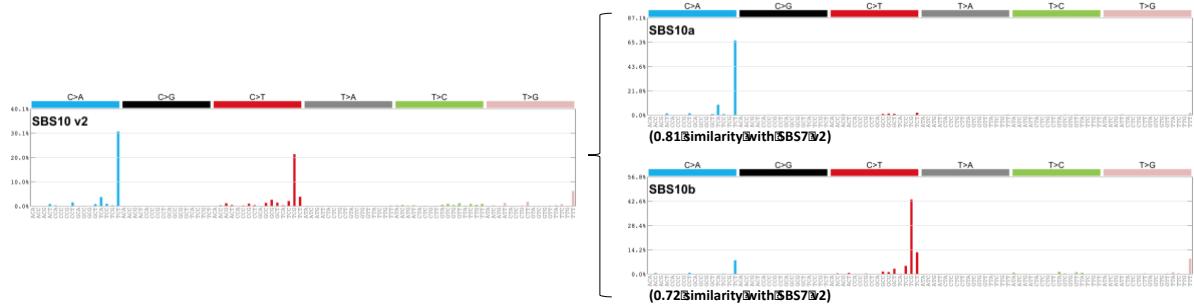
Proposed aetiology

Polymerase epsilon exonuclease domain mutations.

Associated mutation classes and signatures

SBS10b is associated with SBS10a and SBS28 and these signatures are commonly found in the same samples. DBS3 is also associated with SBS10a/b.

Differences between current and previous profiles

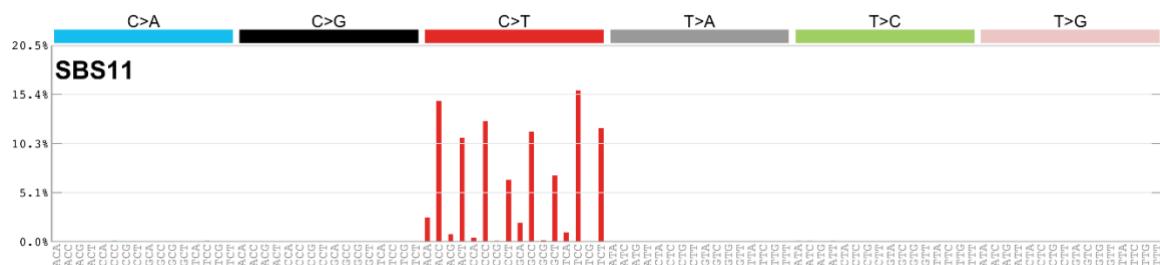


The larger number of analysed samples allows splitting of SBS10 into two distinct components, termed SBS10a/b. SBS28 is also found in most samples with SBS10a/b potentially accounting for the T>G component of the previous SBS10.

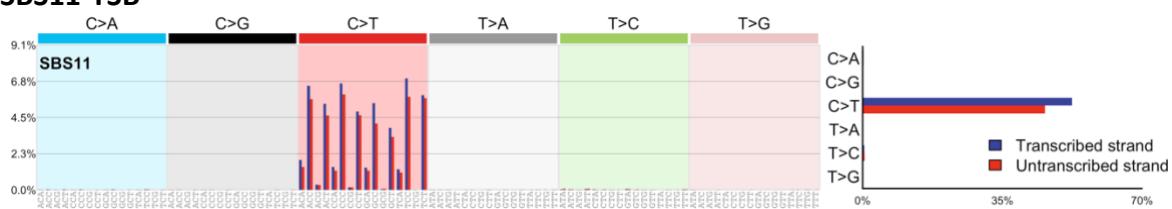
Comments

Signature SBS10a/b usually generate large numbers of somatic mutations (>100 mutations per MB) and samples with these signatures have been termed hypermutators.

SBS11 (v3.0)

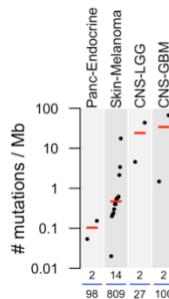


SBS11-TSB



SBS11 exhibits weak transcriptional strand-bias with more mutations of G than C on the untranscribed strands of genes consistent with damage to guanine and repair by transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



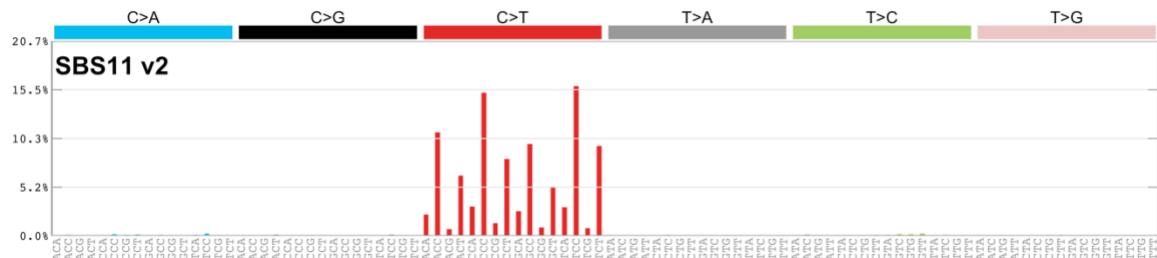
Proposed aetiology

SBS11 exhibits a mutational pattern resembling that of alkylating agents. Patient histories indicate an association between previous treatment with the alkylating agent temozolomide and SBS11 mutations.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

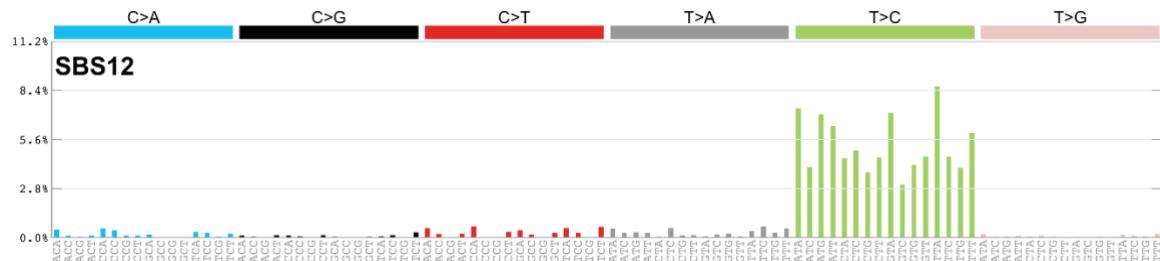


The pattern of SBS11 has been quite stable. The cosine similarity between the prior and current versions of SBS11 is 0.97.

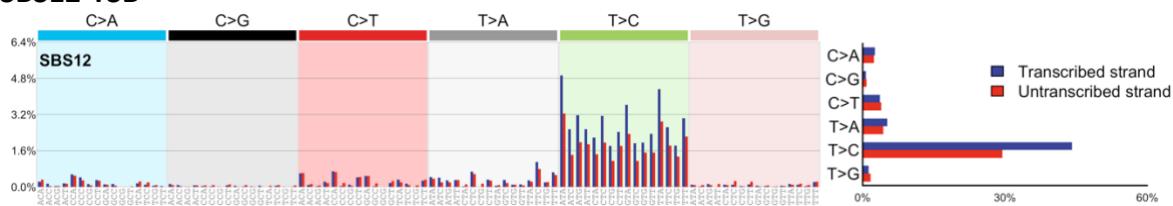
Comments

SBS11 usually generates large numbers of somatic mutations (>10 mutations per MB).

SBS12 (v3.0)

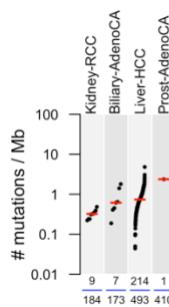


SBS12-TSB



Transcriptional strand-bias for T>C substitutions with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



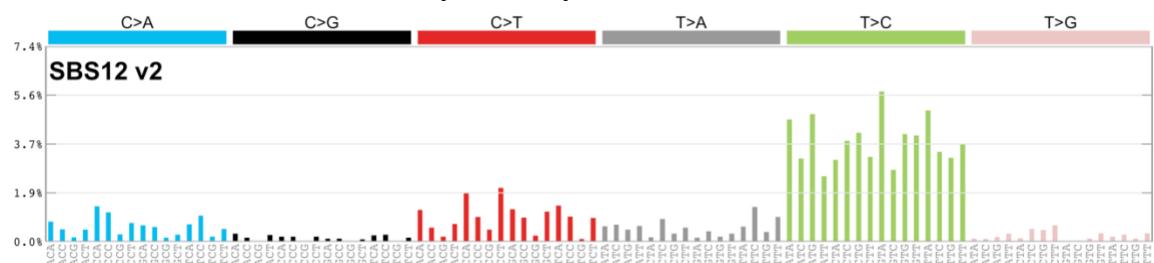
Proposed aetiology

Unknown.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

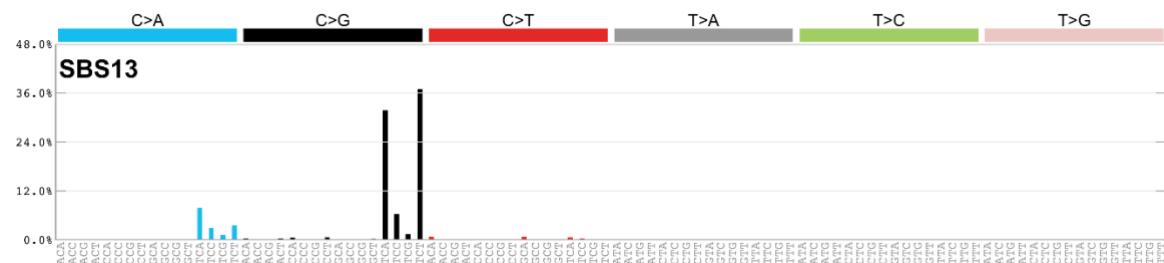


Smaller contributions from C>T and C>A mutations probably reflecting less contamination by other mutational signatures. The cosine similarity between the prior and current versions of SBS12 is 0.94.

Comments:

SBS12 usually contributes a small percentage (<20%) of the mutations observed in liver cancer samples.

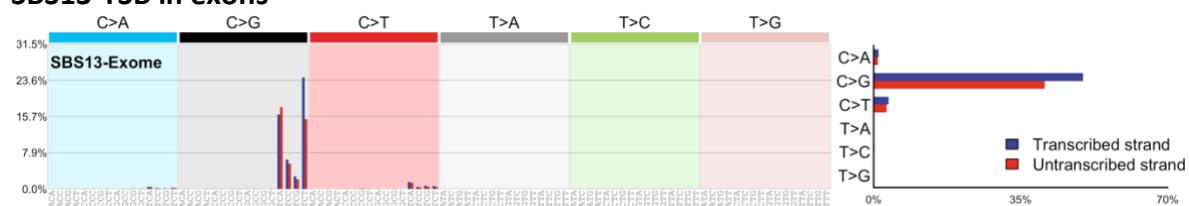
SBS13 (v3.0)



SBS13-TSB

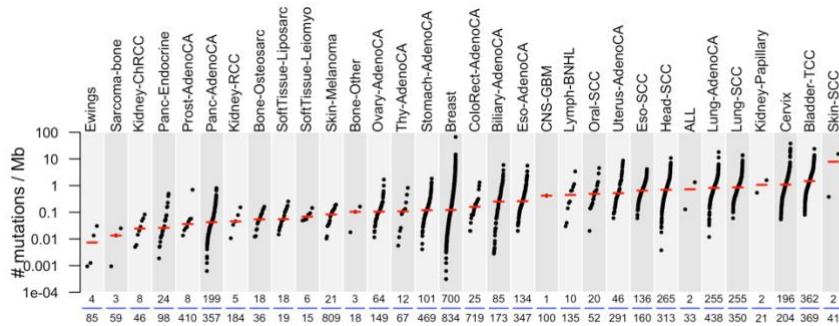


SBS13-TSB in exons



Although there does not appear to be transcriptional strand bias when all transcribed genomic regions are considered (as above), there is transcriptional strand bias of mutations in exons.

Cancer types in which the signature is found



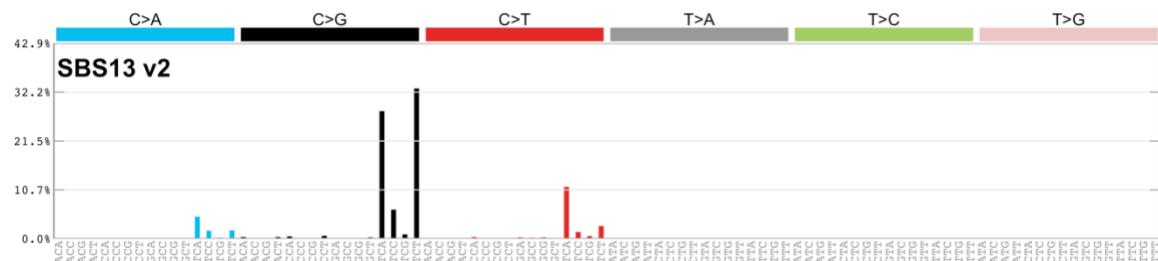
Proposed aetiology

Attributed to activity of the AID/APOBEC family of cytidine deaminases on the basis of similarities in the sequence context of cytosine mutations caused by APOBEC enzymes in experimental systems. APOBEC3A is probably responsible for most mutations in human cancer, although APOBEC3B may also contribute (these differ in the sequence context two bases 5' to the mutated cytosine, see 1536 mutation classification signature extraction). SBS13 mutations are likely generated by error prone polymerases (such as REV1) replicating across abasic sites generated by base excision repair removal of uracil.

Associated mutation classes and signatures

SBS13 is closely associated with SBS2. SBS13 is also associated with DBS11, which is characterised predominantly by CC>TT doublet base substitutions as well as other CC>NN doublet base substitutions.

Differences between current and previous profiles

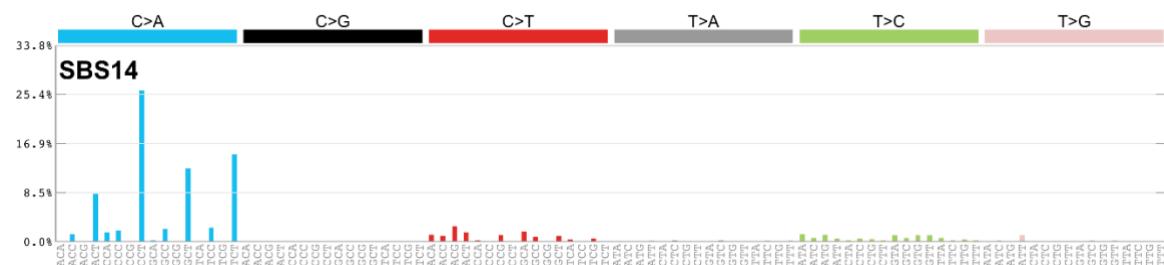


The contribution of C>T mutations at TCN trinucleotides has diminished markedly compared to previous profiles indicating reduced contamination by SBS2. The cosine similarity between the prior and current versions of SBS13 is 0.97.

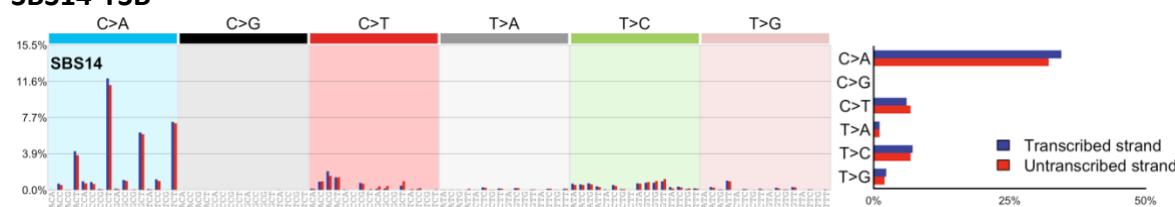
Comments

SBS13 is usually found in the same samples as SBS2. It has been proposed that activation of AID/APOBEC cytidine deaminases in cancer may be due to previous viral infection, retrotransposon jumping, or tissue inflammation. Currently, there is limited evidence to support these hypotheses. Germline polymorphisms involving APOBEC3A and APOBEC3B are associated with predisposition to breast and bladder cancer as well as with mutation burdens of SBS2 and SBS13. Mutations of similar patterns to SBS2 and SBS13 are commonly found in the phenomenon of local hypermutation present in some cancers, known as kataegis, implicating AID/APOBEC enzymes in this process as well.

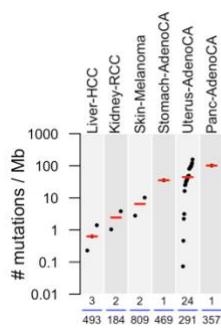
SBS14 (v3.0)



SBS14-TSB



Cancer types in which the signature is found



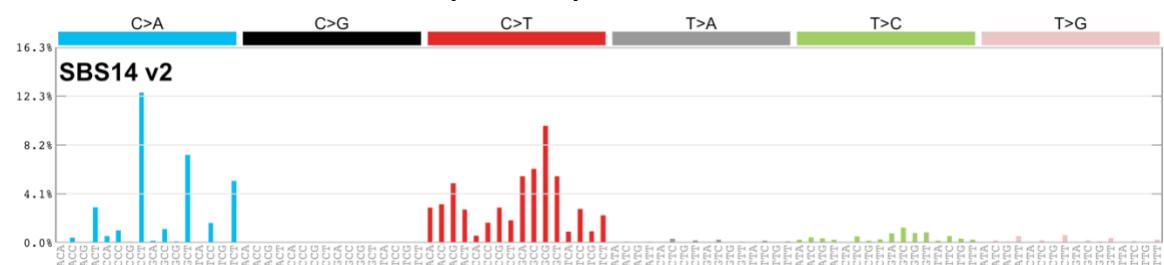
Proposed aetiology

Concurrent polymerase epsilon mutation and defective DNA mismatch repair.

Associated mutation classes and signatures

SBS14 is associated with ID1 and ID2.

Differences between current and previous profiles

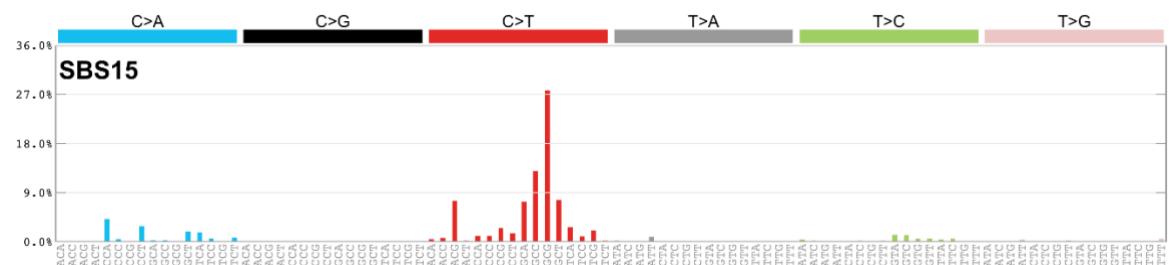


The pattern of SBS14 has changed extensively with C>A mutations separating from C>T mutations. Please note that the pattern of C>T mutations in the prior version of SBS14 was most likely a contamination from SBS6. The cosine similarity between the prior and current versions of SBS14 is 0.74.

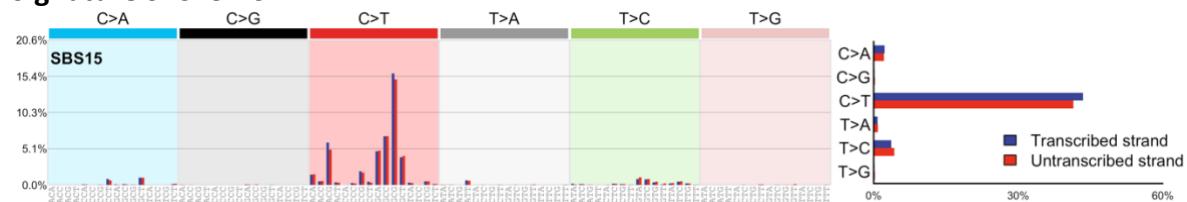
Comments

SBS14 mutations are present in very high numbers in all samples in which it has been observed. SBS14 is one of seven mutational signatures associated with defective DNA mismatch repair (MSI) and is often found in the same samples as other MSI associated signatures: SBS6, SBS15, SBS20, SBS21, SBS26 and SBS44.

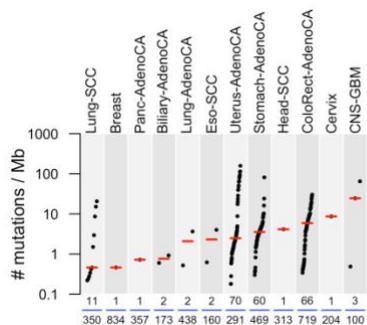
SBS15 (v3.0)



Signature SBS15-TSB



Cancer types in which the signature is found



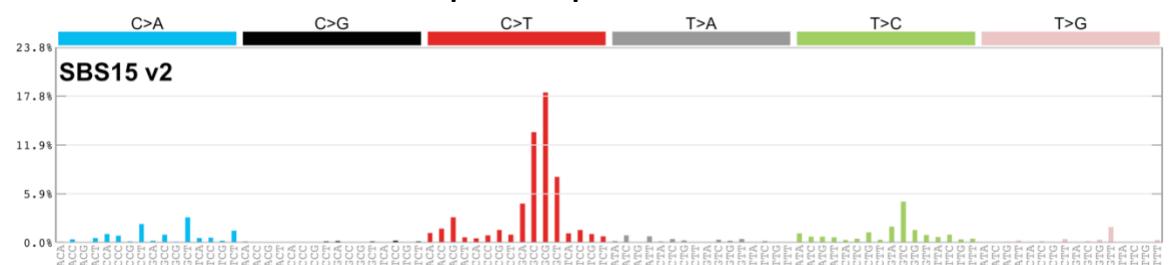
Proposed aetiology

Defective DNA mismatch repair.

Associated mutation classes and signatures

SBS15 is associated with ID1 and ID2.

Differences between current and previous profiles

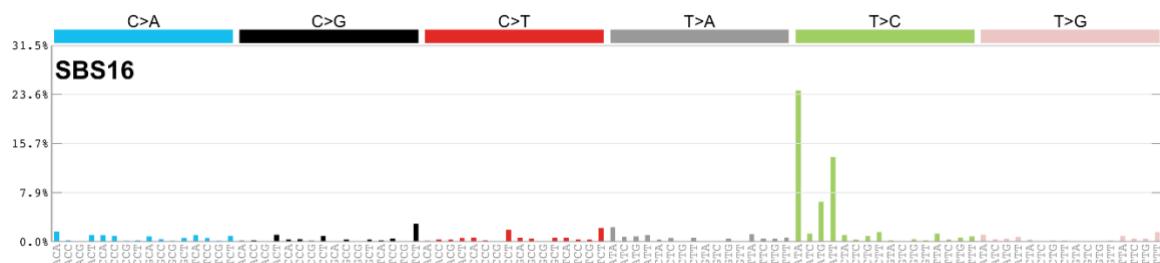


Smaller contributions of C>A and T>C mutations indicating less contamination by other DNA mismatch repair deficiency signatures. The cosine similarity between the prior and current versions of SBS15 is 0.94.

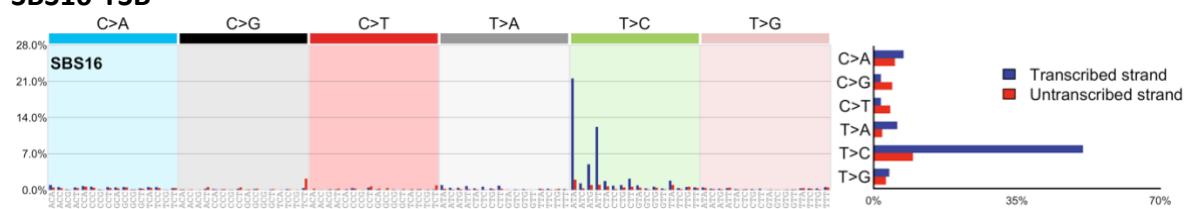
Comments

SBS15 is one of seven mutational signatures associated with defective DNA mismatch repair (MSI) and is often found in the same samples as other MSI associated signatures: SBS6, SBS14, SBS20, SBS21, SBS26, and SBS44.

SBS16 (v3.0)

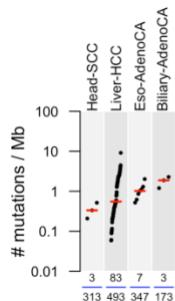


SBS16-TSB



Extremely strong transcriptional strand bias of T>C mutations at ATN trinucleotides with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription coupled nucleotide excision repair. There is also evidence for SBS16 of transcription coupled DNA damage, with more damage to A on untranscribed than on transcribed strands (in addition to transcription coupled nucleotide excision repair).

Cancer types in which the signature is found



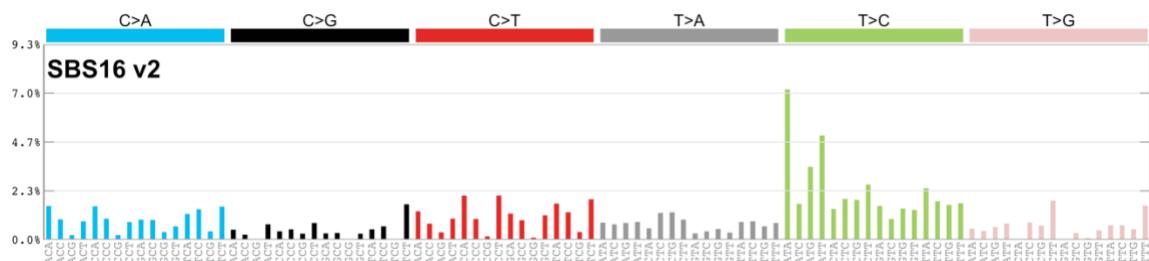
Proposed aetiology

Unknown.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

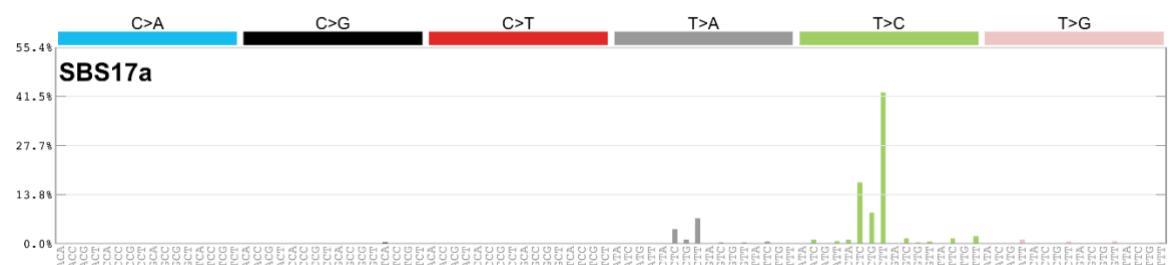


The profile of SBS16 exhibits less contamination by other mutation signatures, notably SBS5 and SBS12. The cosine similarity between the prior and current versions of SBS16 is 0.79.

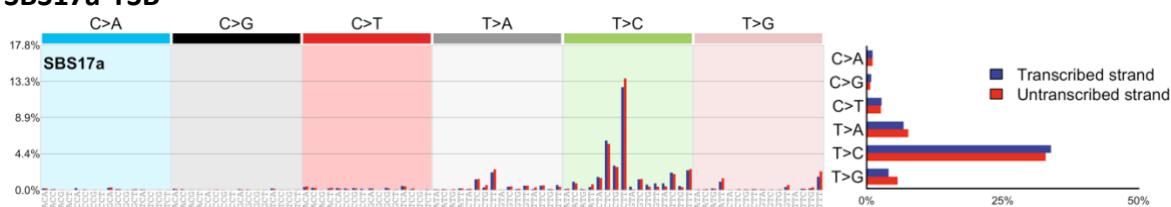
Comments

In addition to lower levels of nucleotide excision repair on the untranscribed strands of genes, elevated levels of DNA damage on untranscribed strands (compared to the remainder of the genome) may contribute to SBS16. Contamination by SBS16 may still be present in the current version of SBS5.

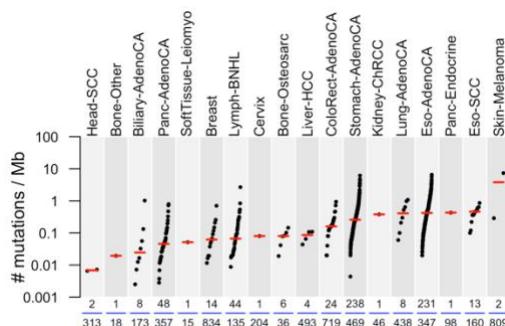
SBS17a (v3.0)



SBS17a-TSB



Cancer types in which the signature is found



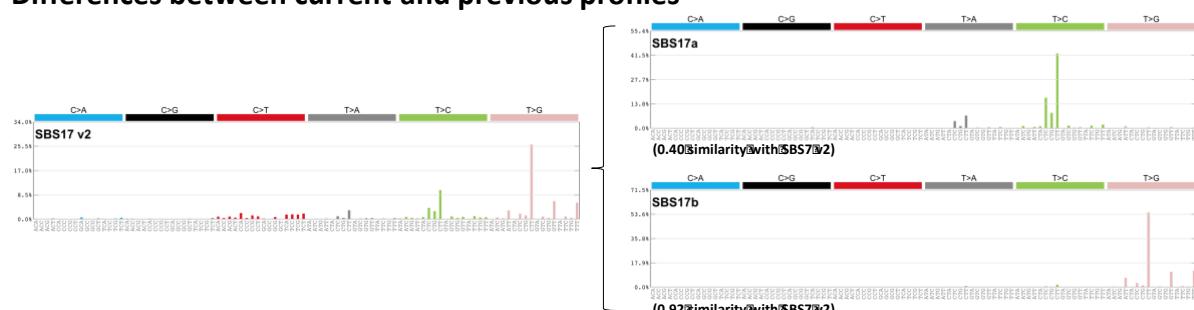
Proposed aetiology

Unknown.

Associated mutation classes and signatures

SBS17a is associated with SBS17b and these signatures are commonly found in the same samples.

Differences between current and previous profiles

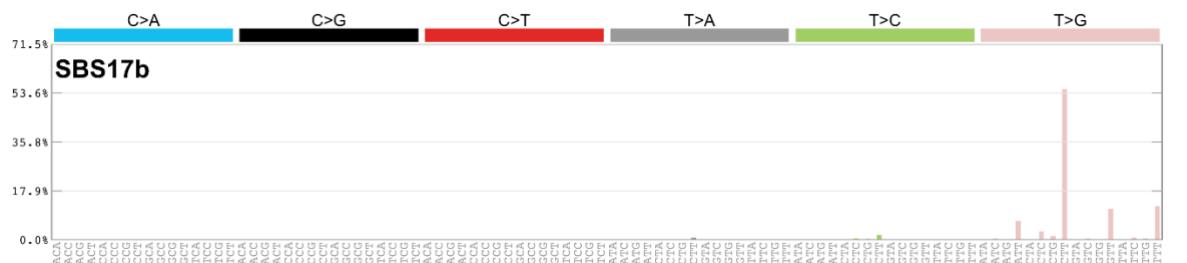


The larger number of analysed samples allow splitting of SBS17 into two distinct components, termed, SBS17a/b, that together almost perfectly recapitulate the original signature.

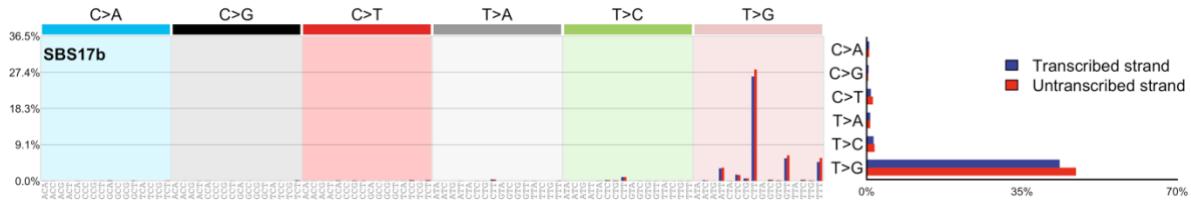
Comments

SBS17b has similarities to SBS28 and these two signatures can be mistaken for one another.

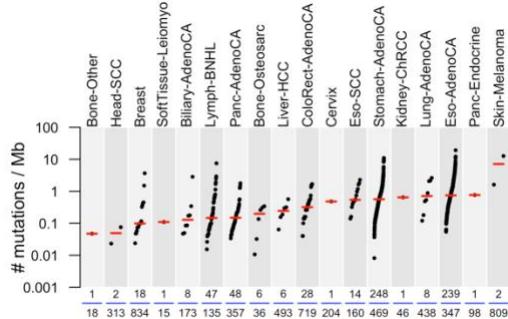
SBS17b (v3.0)



SBS17b-TSB



Cancer types in which the signature is found



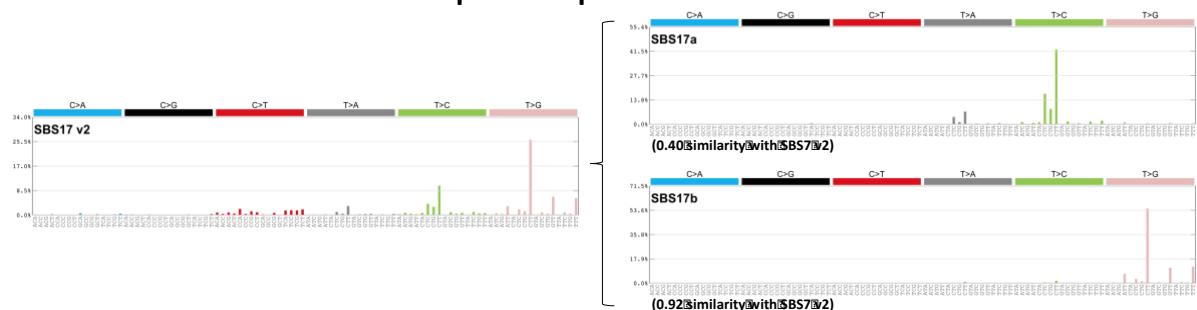
Proposed aetiology

Unknown.

Associated mutation classes and signatures

SBS17b is associated with SBS17a and these signatures are commonly found in the same samples.

Differences between current and previous profiles

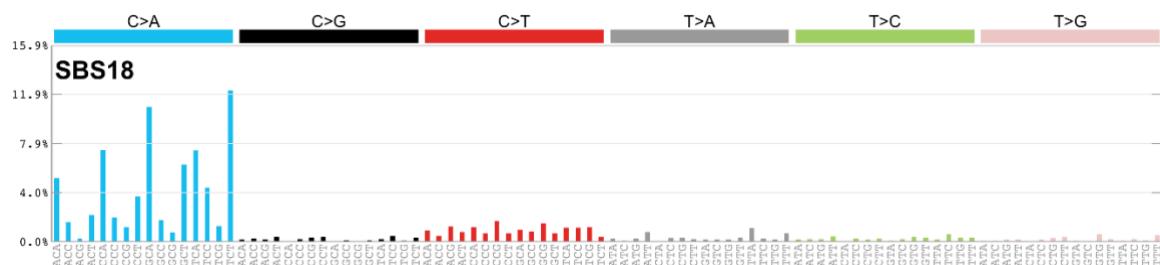


The larger number of analysed samples allows splitting of SBS17 into two distinct components, termed SBS17a/b, that together recapitulate the original signature.

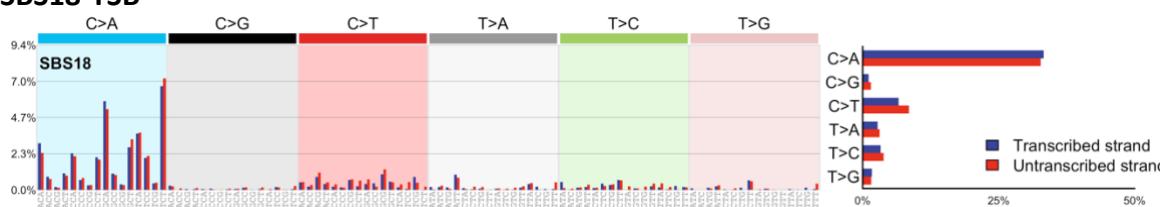
Comments

N/A

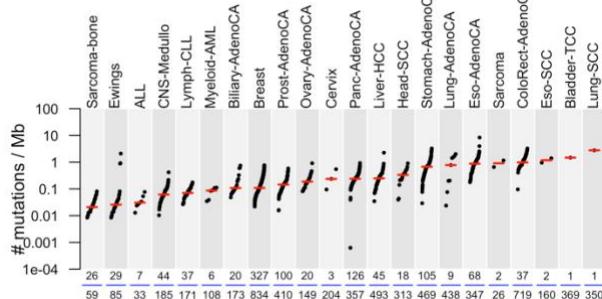
SBS18 (v3.0)



SBS18-TSB



Cancer types in which the signature is found



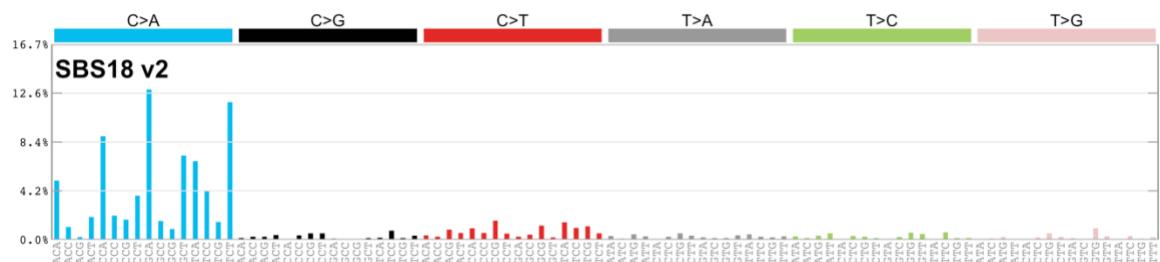
Proposed aetiology

Possibly damage by reactive oxygen species.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

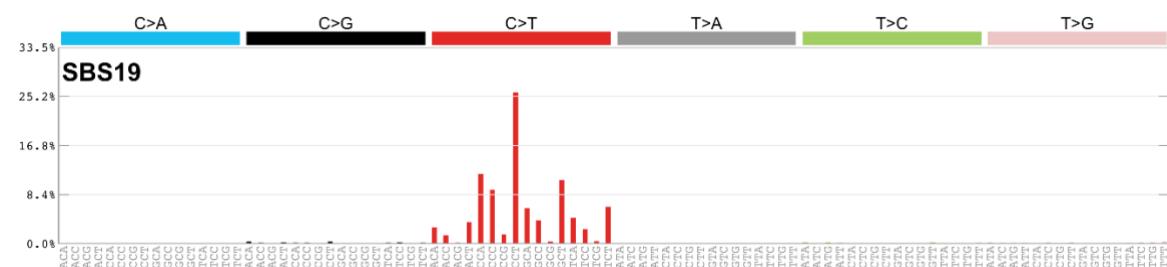


The cosine similarity between the prior and current versions of SBS18 is 0.99.

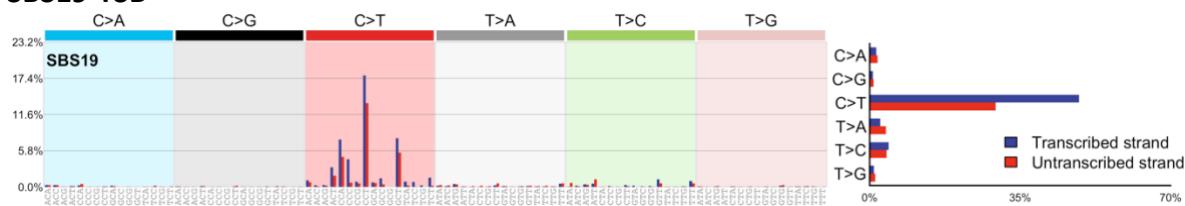
Comments

Similar in profile to SBS36 which is associated with defective base excision repair due to *MUTYH* mutations.

SBS19 (v3.0)

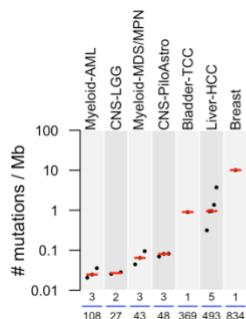


SBS19-TSB



Transcriptional strand bias of C>T mutations with more mutations of G than C on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



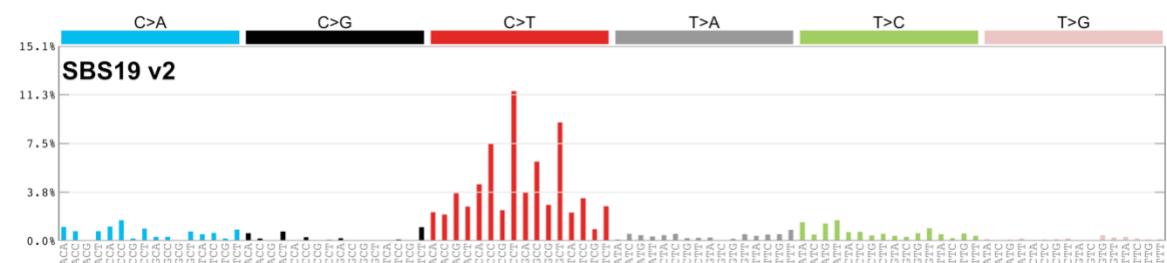
Proposed aetiology

Unknown.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

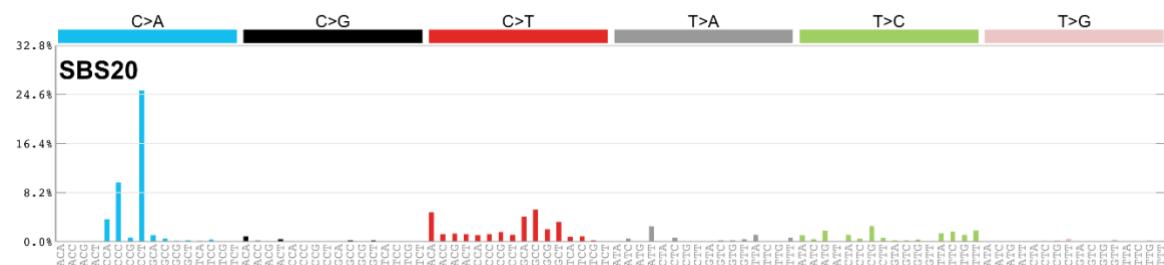


Reduced contamination by other mutational signatures especially SBS1 and SBS5. The cosine similarity between the prior and current versions of SBS19 is 0.89.

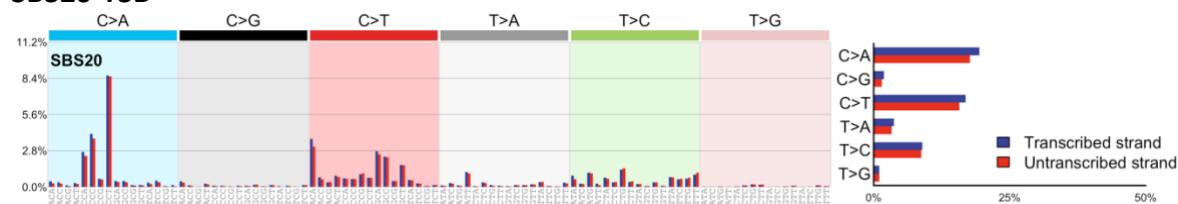
Comments

N/A

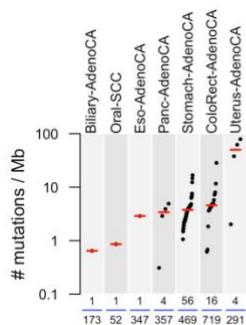
SBS20 (v3.0)



SBS20-TSB



Cancer types in which the signature is found



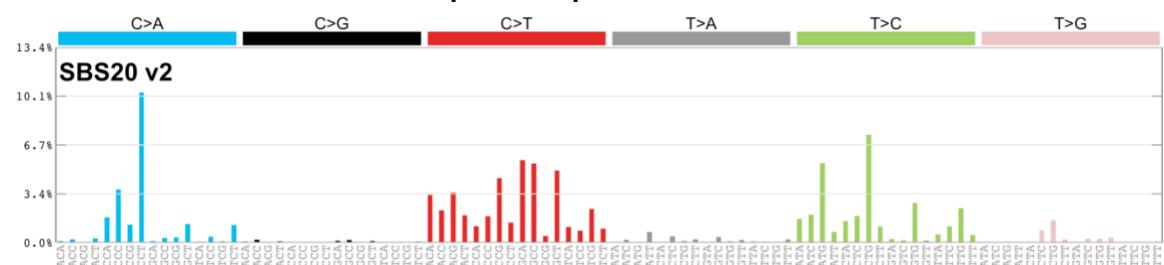
Proposed aetiology

Concurrent POLD1 mutations and defective DNA mismatch repair.

Associated mutation classes and signatures

SBS20 is associated ID1 and ID2.

Differences between current and previous profiles

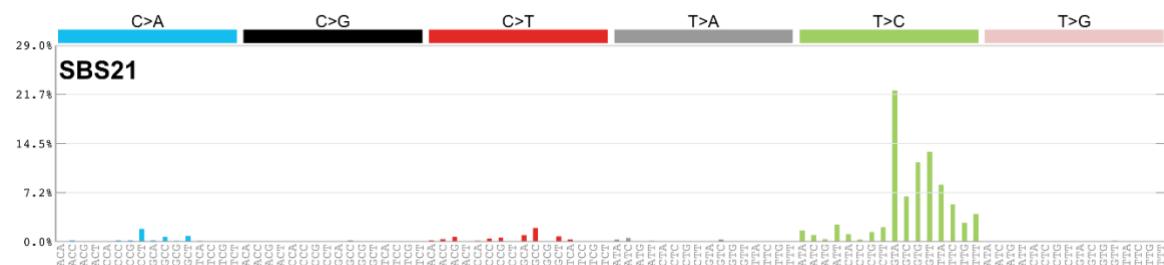


Reduced contamination by other DNA mismatch deficiency signatures. The cosine similarity between the prior and current versions of SBS20 is 0.78.

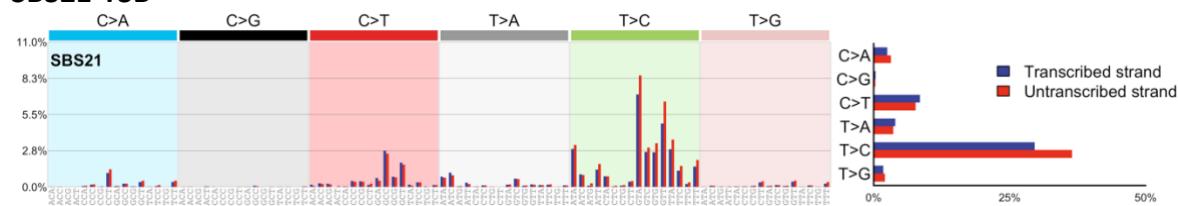
Comments

SBS20 is one of seven mutational signatures associated with defective DNA mismatch repair (MSI) and is often found in the same samples as other MSI associated signatures: SBS6, SBS14, SBS15, SBS21, SBS26, and SBS44.

SBS21 (v3.0)

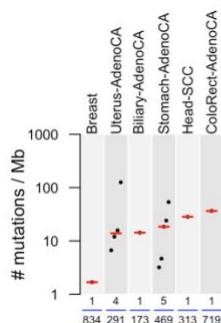


SBS21-TSB



Transcriptional strand bias with more mutated T than A on untranscribed strands of genes compatible with damage to thymidine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



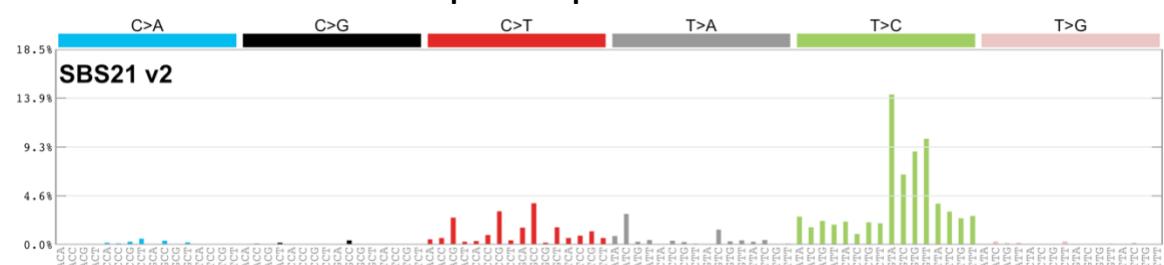
Proposed aetiology

DNA mismatch repair deficiency.

Associated mutation classes and signatures

SBS21 is associated with ID1 and ID2.

Differences between current and previous profile

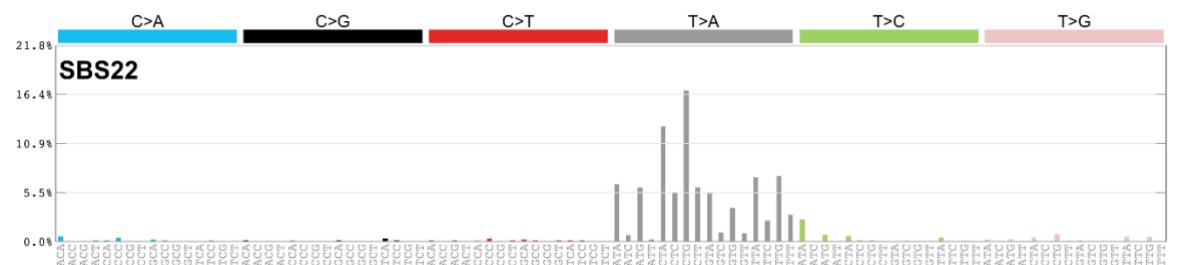


Reduced contamination by other signatures of DNA mismatch repair deficiency. The cosine similarity between the prior and current versions of SBS21 is 0.95.

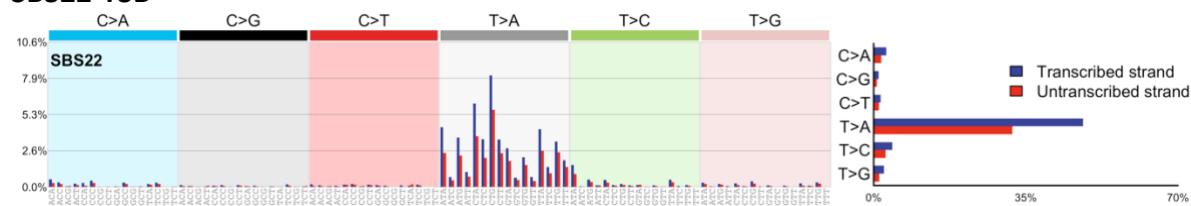
Comments

SBS21 is one of seven mutational signatures associated with defective DNA mismatch repair (MSI) and is often found in the same samples as other MSI associated signatures: SBS6, SBS14, SBS15, SBS20, SBS26, and SBS44.

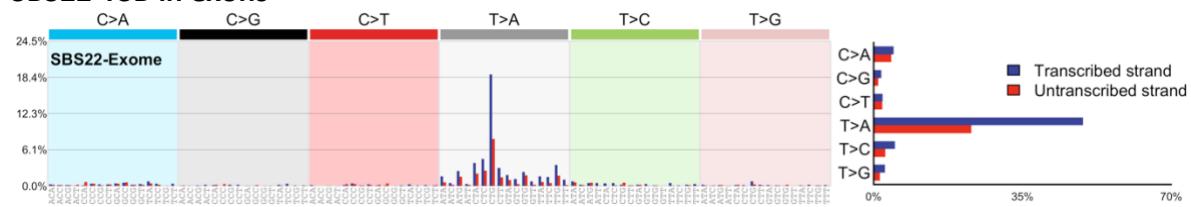
SBS22 (v3.0)



SBS22-TSB

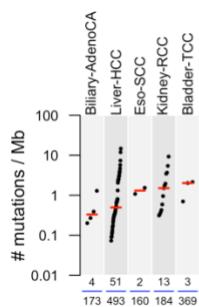


SBS22-TSB in exons



SBS22 exhibits strong transcriptional strand bias for T>A mutations with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription-coupled nucleotide excision repair. The transcriptional strand bias also exists in exonic regions.

Cancer types in which the signature is found



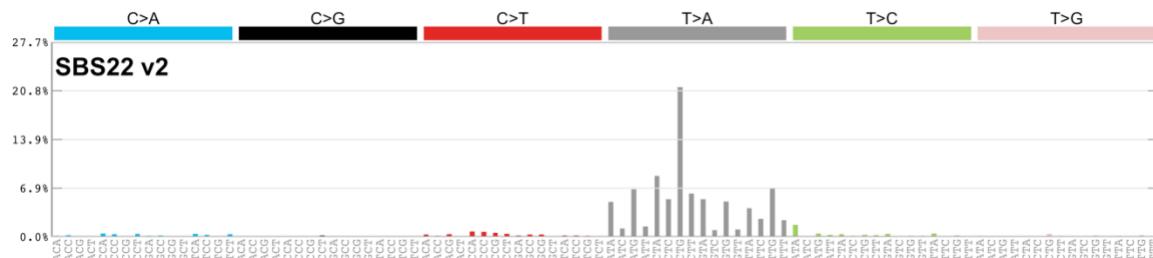
Proposed aetiology

Aristolochic acid exposure. Found in cancer samples with known exposures to aristolochic acid and the pattern of mutations exhibited by the signature is consistent with that observed in experimental systems of aristolochic acid exposure.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

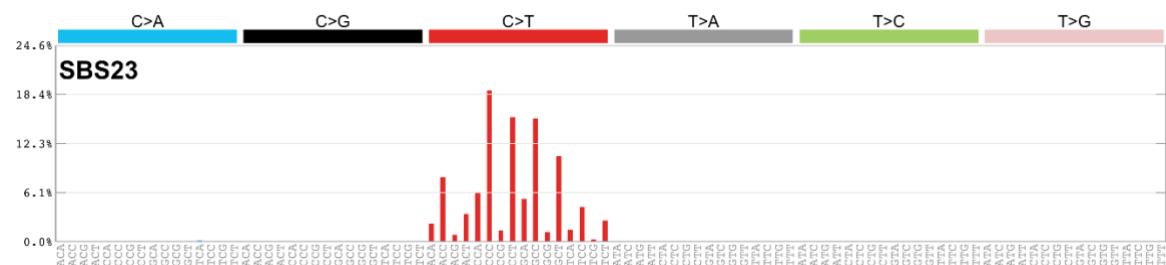


The cosine similarity between the prior and current versions of SBS22 is 0.96.

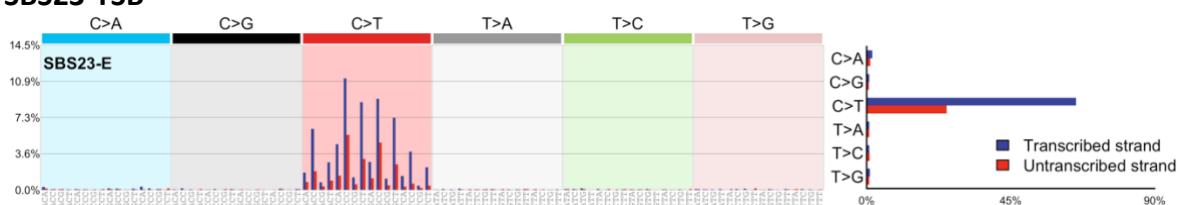
Comments

N/A

SBS23 (v3.0)

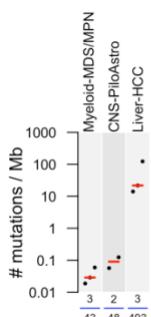


SBS23-TSB



SBS23 exhibits strong transcriptional strand bias for C>T mutations with more mutations of G than C on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair. Please note that SBS23 has only been found in exome sequencing data and, as such, the transcriptional strand bias reflects the one observed in the coding regions of the genome.

Cancer types in which the signature is found



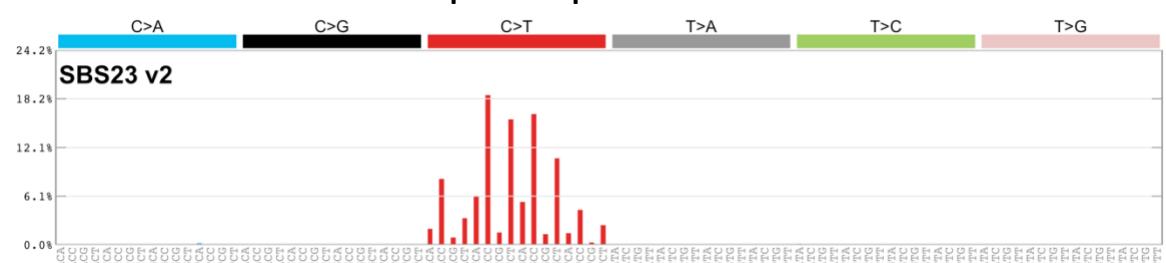
Proposed aetiology

Unknown.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

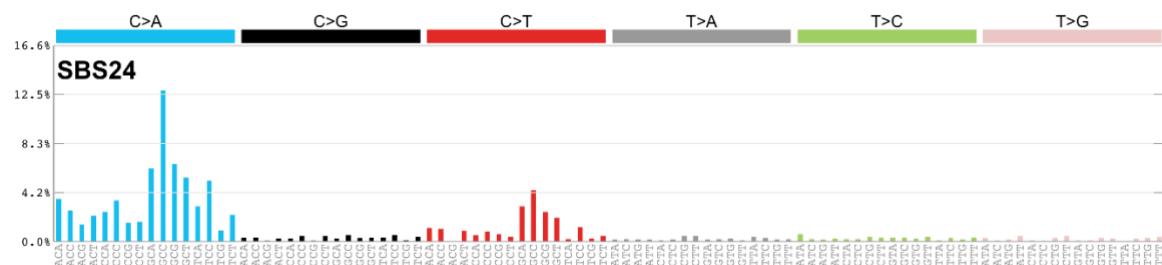


The cosine similarity between the prior and current versions of SBS23 is 1.00.

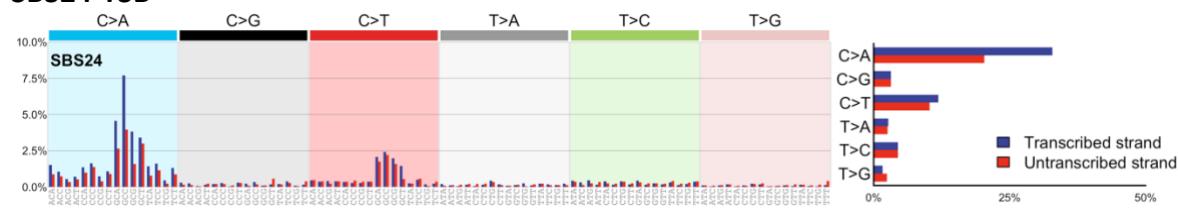
Comments

N/A

SBS24 (v3.0)

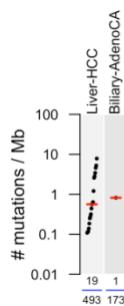


SBS24-TSB



SBS24 exhibits strong transcriptional strand bias for C>A mutations with more mutations of G than C on the untranscribed strands of genes consistent with damage to guanine and repair by transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



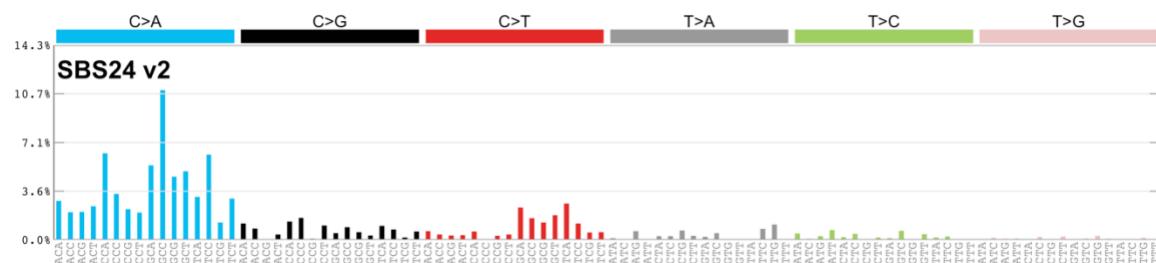
Proposed aetiology

Aflatoxin exposure. SBS24 has been found in cancer samples with known exposures to aflatoxin and the pattern of mutations exhibited by the signature is consistent with that observed in experimental systems exposed to aflatoxin.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

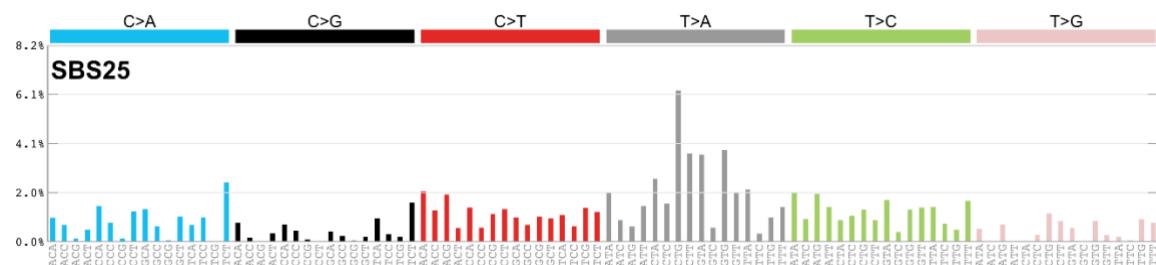


The cosine similarity between the prior and current versions of SBS24 is 0.94.

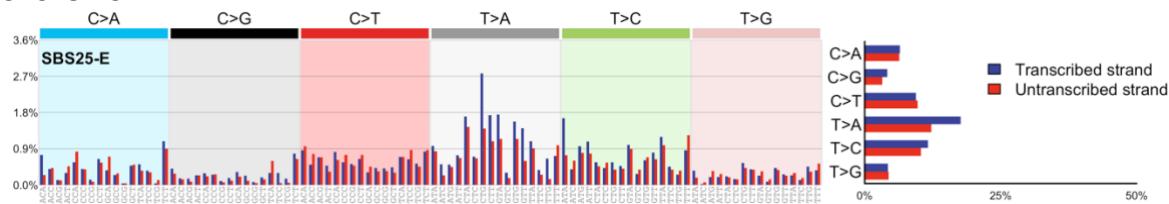
Comments

N/A

SBS25 (v3.0)



SBS25-TSB



Transcriptional strand bias for T>A mutations with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription coupled nucleotide excision repair. Please note that signature SBS25 has only been found in exome sequencing data of cancer cell lines and, as such, the transcriptional strand bias reflects that observed in the coding regions of the genome.

Cancer types in which the signature is found

Hodgkin lymphoma cell lines

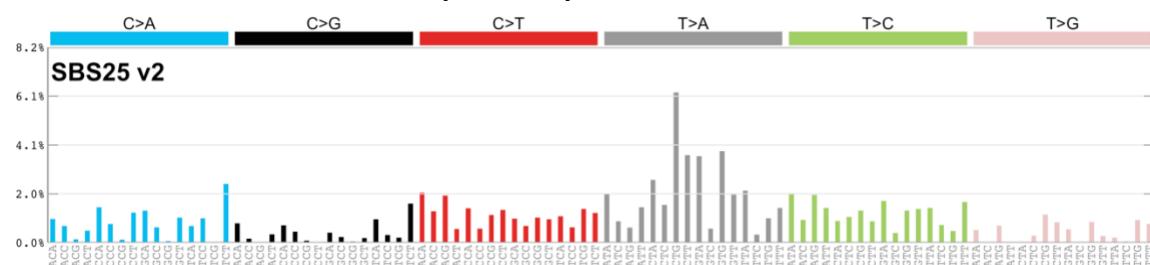
Proposed aetiology

Unknown. However, some Hodgkin's cell line samples in which the signature has been found were from patients exposed to chemotherapy and it is possible that SBS25 is due to chemotherapy treatment.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

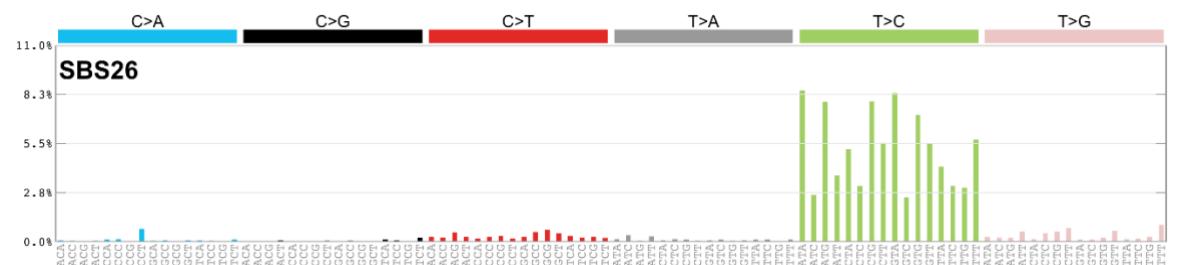


The cosine similarity between the prior and current versions of signature SBS25 is 1.00.

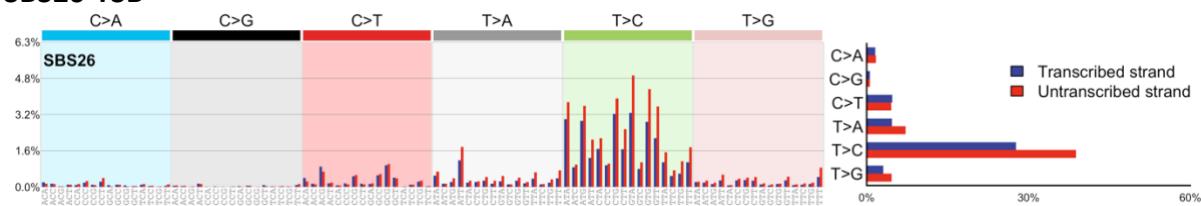
Comments

This signature has only been identified in Hodgkin's cell lines. Data is not available from primary Hodgkin lymphomas.

SBS26 (v3.0)

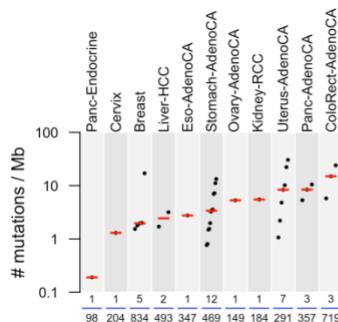


SBS26-TSB



Transcriptional strand bias with more mutated T than A on untranscribed strands of genes compatible with damage to thymidine and activity of transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



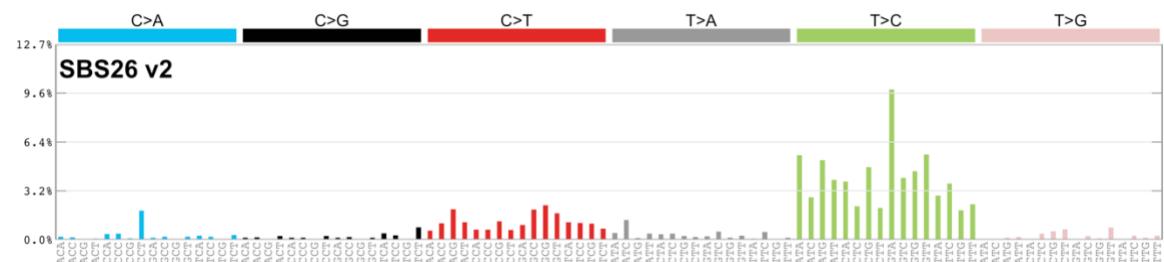
Proposed aetiology

Defective DNA mismatch repair.

Associated mutation classes and signatures

SBS26 is associated ID1 and ID2.

Differences between current and previous profiles

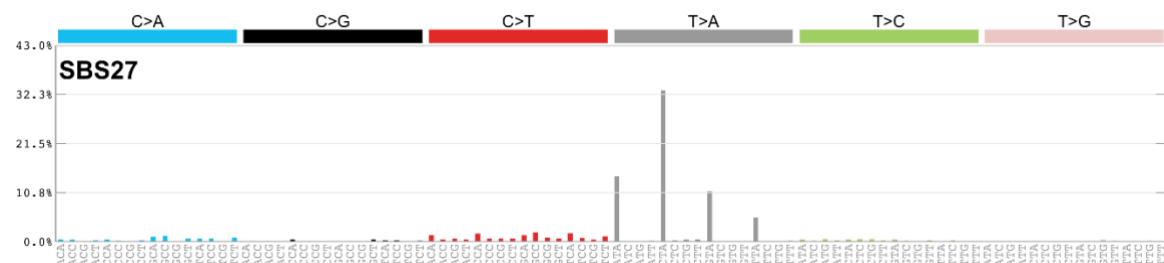


Reduced contamination by other signatures of defective DNA mismatch repair. The cosine similarity between the prior and current versions of SBS26 is 0.92.

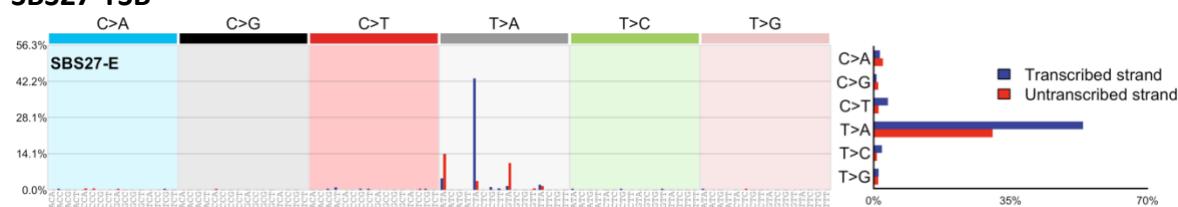
Comments

SBS26 is one of seven mutational signatures associated with defective DNA mismatch repair (MSI) and is often found in the same samples as other MSI associated signatures: SBS6, SBS14, SBS15, SBS20, SBS21, and SBS44.

SBS27 (v3.0)

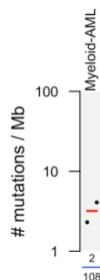


SBS27-TSB



Signature 27 exhibits strong transcriptional strand bias for T>A mutations with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription couple nucleotide excision repair and/or DNA damage. However, the transcriptional strand bias is inconsistent across trinucleotide contexts. Please note that signature SBS27 has only been found in exome sequencing data and, as such, the transcriptional strand bias reflects the one observed in the coding regions of the genome.

Cancer types in which the signature is found



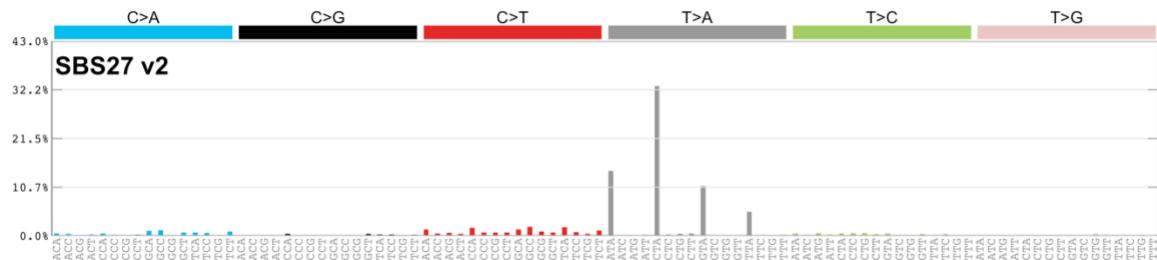
Proposed aetiology

Possible sequencing artefact.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

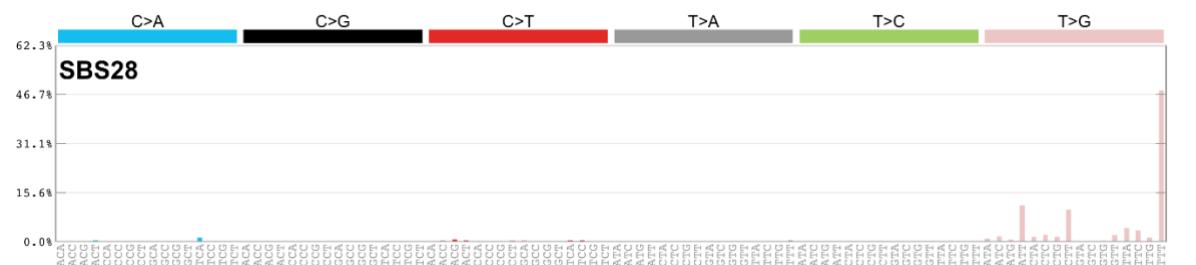


The cosine similarity between the prior and current versions of signature SBS27 is 1.00.

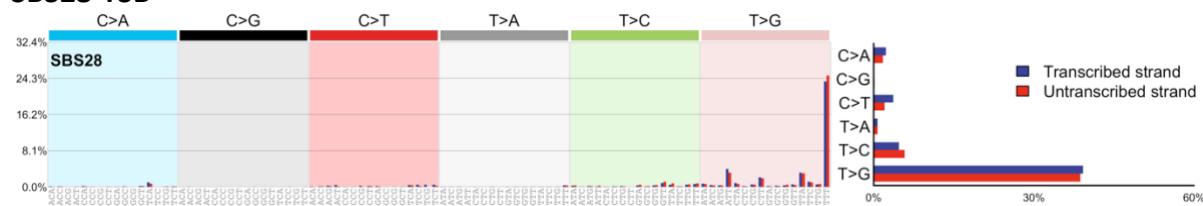
Comments

N/A

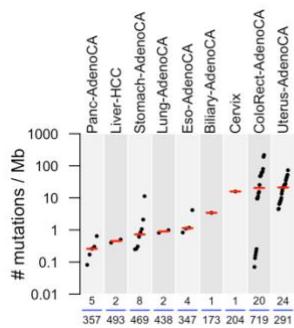
SBS28 (v3.0)



SBS28-TSB



Cancer types in which the signature is found



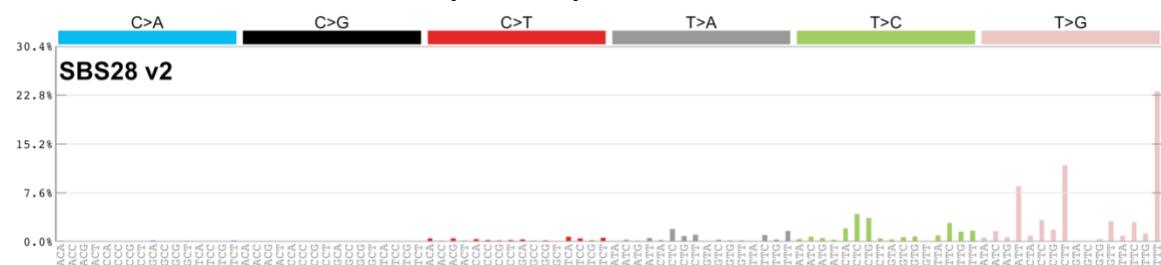
Proposed aetiology

Unknown.

Associated mutation classes and signatures

SBS28 is found in most samples with SBS10a/b.

Differences between current and previous profiles

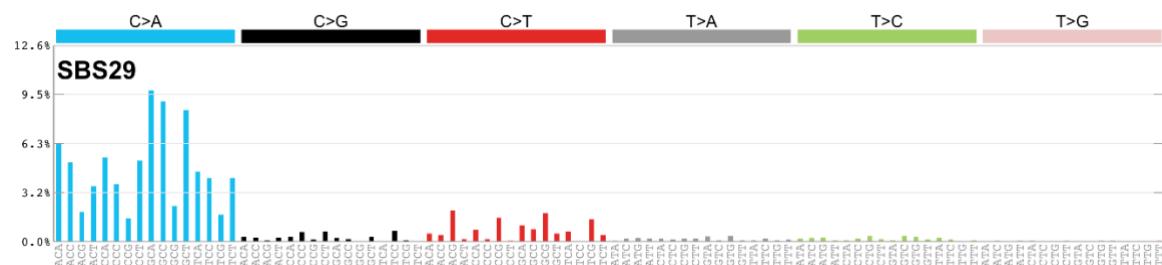


The cosine similarity between the prior and current versions of signature SBS28 is 0.92.

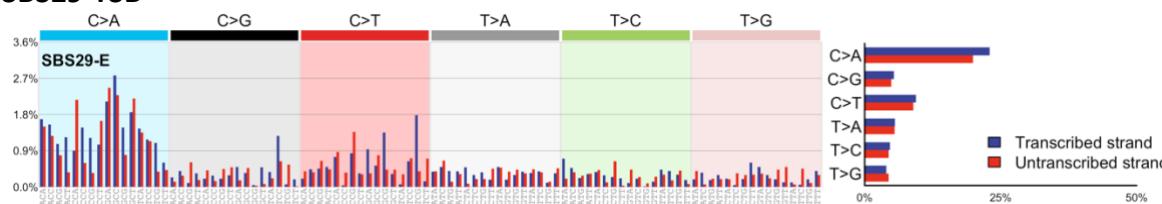
Comments

SBS28 has similarities to SBS17b and these two signatures can be mistaken for one another. Signature SBS28 is found in most samples with SBS10a/b where it contributes very high numbers of mutations. In contrast, SBS28 contributes much smaller number of mutations in samples lacking SBS10a/b.

SBS29 (v3.0)

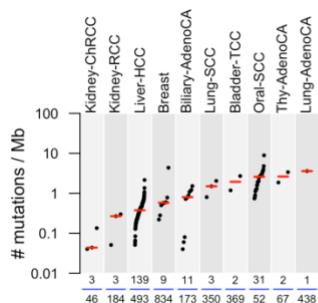


SBS29-TSB



SBS29 exhibits weak transcriptional strand bias for C>A mutations indicating guanine damage that is most likely repaired by transcription-coupled nucleotide excision repair. Please note that SBS29 has only been found in exome sequencing data and, as such, the transcriptional strand bias reflects the one observed in the coding regions of the genome.

Cancer types in which the signature is found



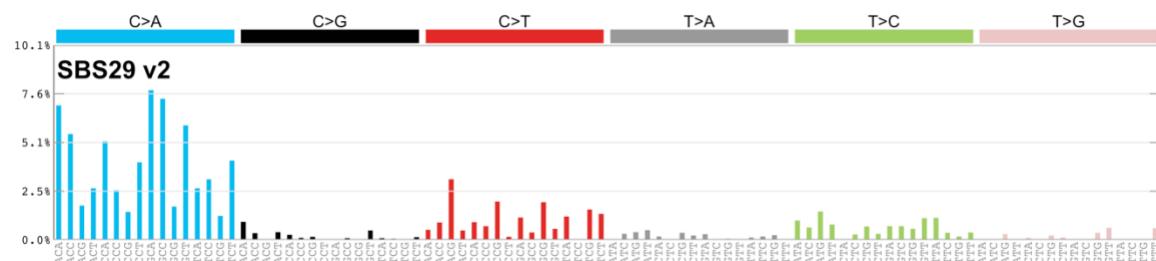
Proposed aetiology

SBS29 has been found in cancer samples from individuals with a tobacco chewing habit.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

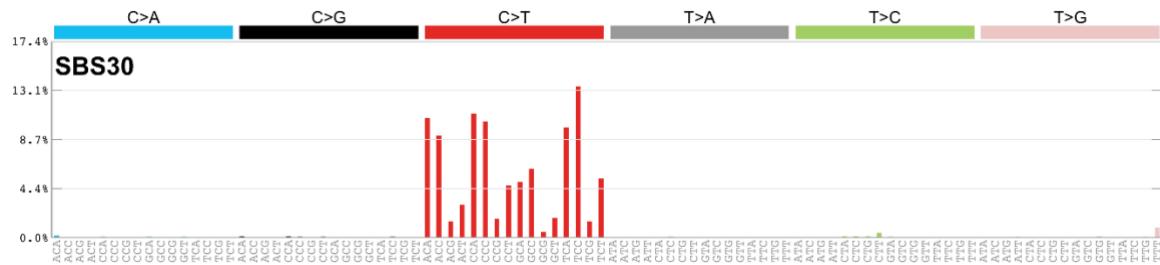


The cosine similarity between the prior and current versions of SBS29 is 0.97.

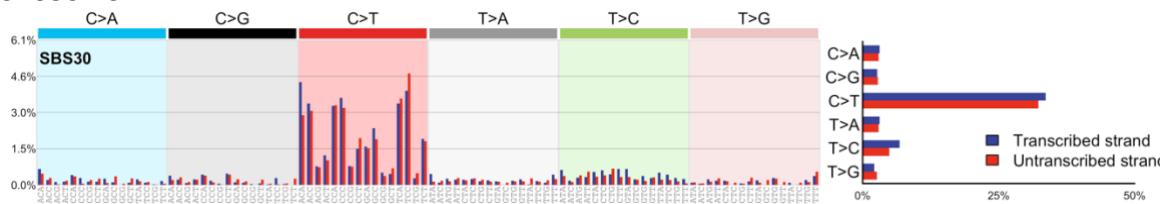
Comments

The pattern of C>A mutations in SBS29 appears different from the pattern of mutations due to tobacco smoking reflected by SBS4.

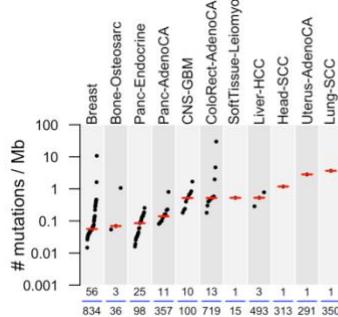
SBS30(v3.0)



SBS30-TSB



Cancer types in which the signature is found



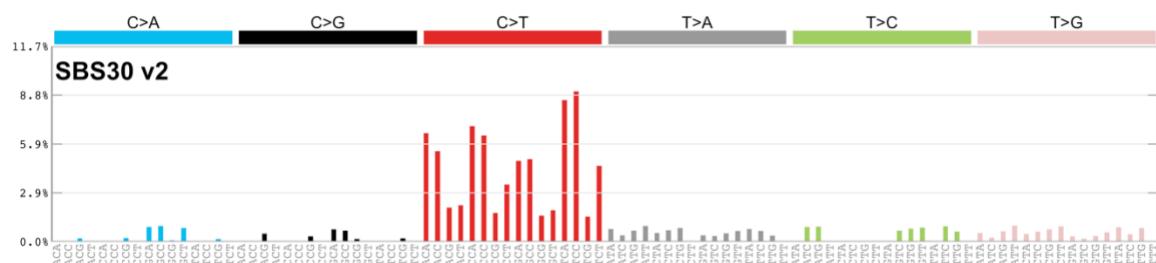
Proposed aetiology

SBS30 is due to deficiency in base excision repair due to inactivating mutations in *NTHL1*.

Associated mutation classes and signatures

N/A

Differences between current and previous profiles

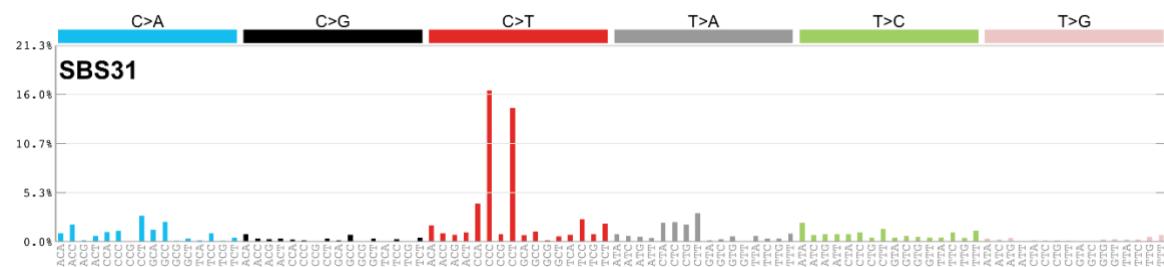


The cosine similarity between the prior and current versions of signature SBS30 is 0.96.

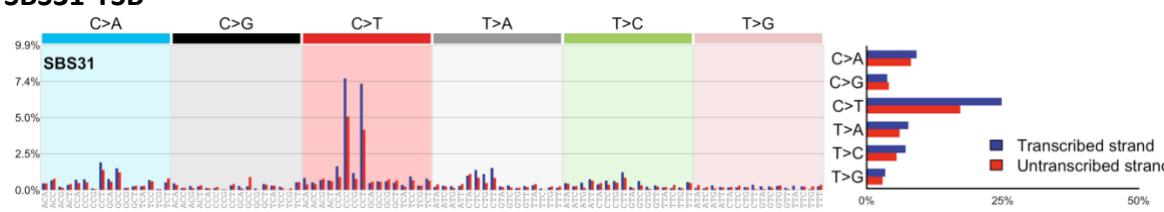
Comments

N/A

SBS31 (v3.0)

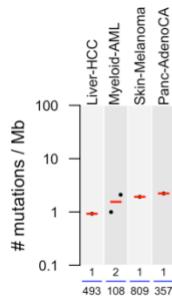


SBS31-TSB



Transcriptional strand bias of C>T mutations with more G than C mutations on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Prior chemotherapy treatment with platinum drugs.

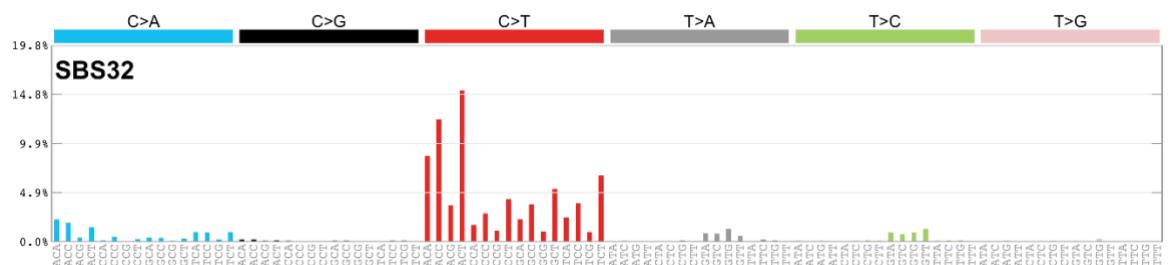
Associated mutation classes and signatures

SBS31 is associated with DBS5, which is predominantly characterized with CT>AA mutations.

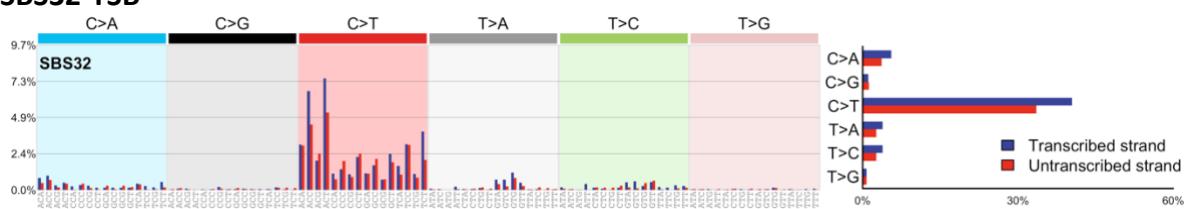
Comments

SBS31 exhibits a pattern of mutations similar to components of SBS35 and both may be due to platinum drug treatment.

SBS32 (v3.0)

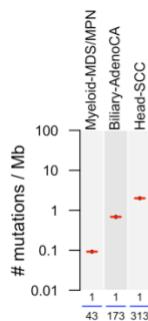


SBS32-TSB



Transcriptional strand bias of C>T mutations with more G than C mutations on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

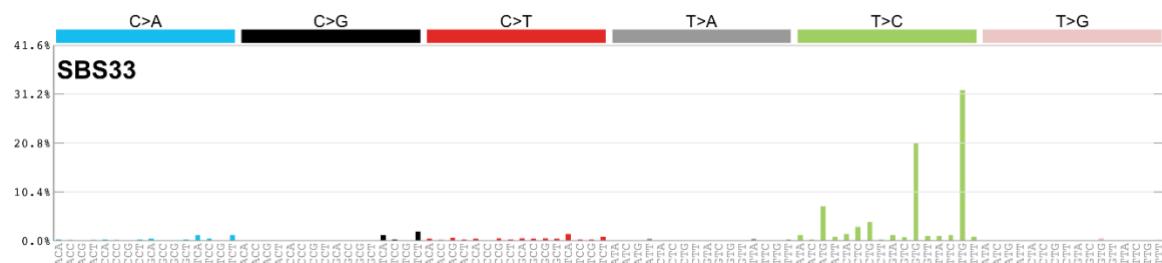
Prior treatment with azathioprine to induce immunosuppression. **Associated mutation classes and signatures**

N/A

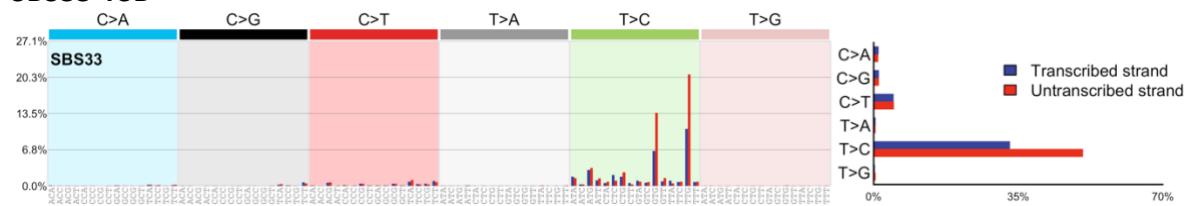
Comments

N/A

SBS33 (v3.0)

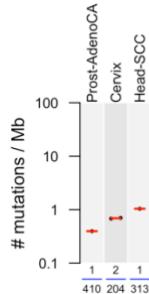


SBS33-TSB



Transcriptional strand bias of T>C mutations with more T than A mutations on untranscribed strands of gene consistent with damage to thymidine and transcriptional coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Unknown.

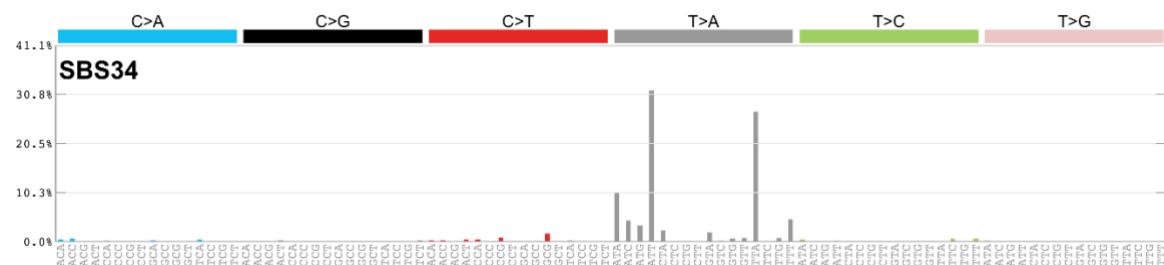
Associated mutation classes and signatures

N/A

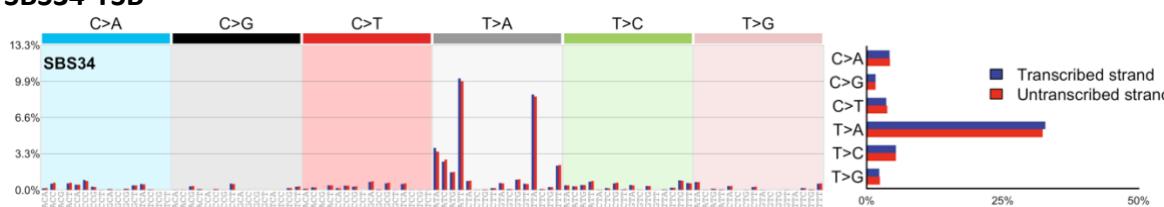
Comments

N/A

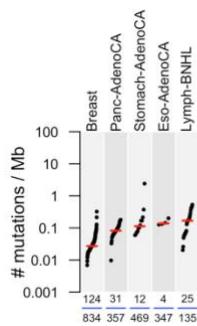
SBS34 (v3.0)



SBS34-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown.

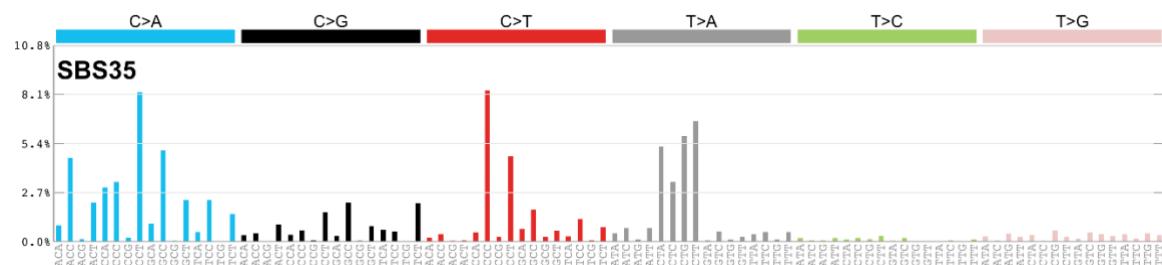
Associated mutation classes and signatures

N/A

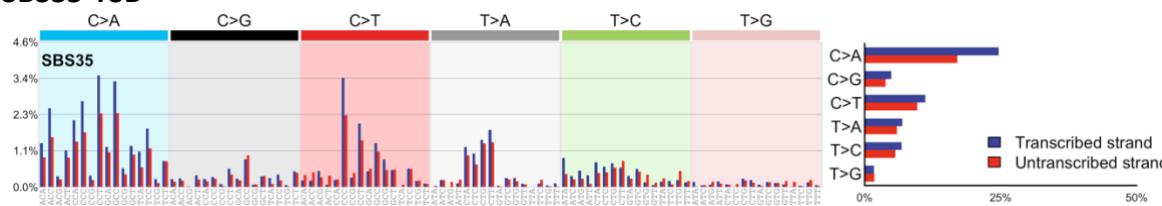
Comments

N/A

SBS35 (v3.0)

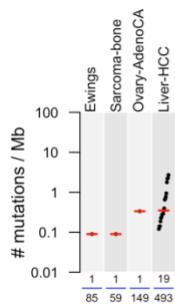


SBS35-TSB



Transcriptional strand bias of C>A and C>T mutations with more G than C mutations on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Prior chemotherapy treatment with platinum drugs.

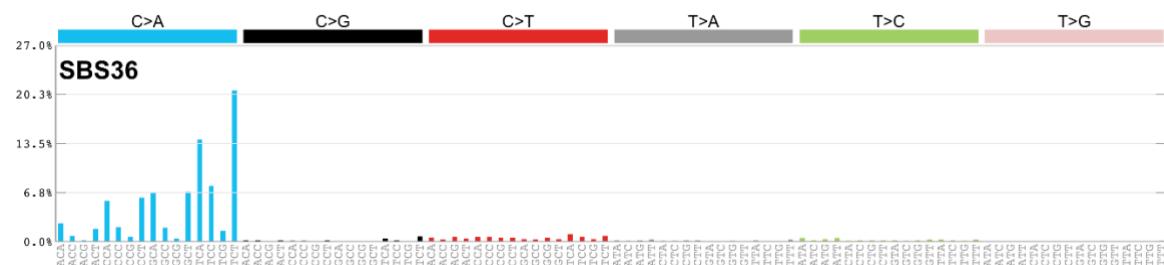
Associated mutation classes and signatures

SBS35 is associated with DBS5, which is predominantly characterized with CT>AA mutations.

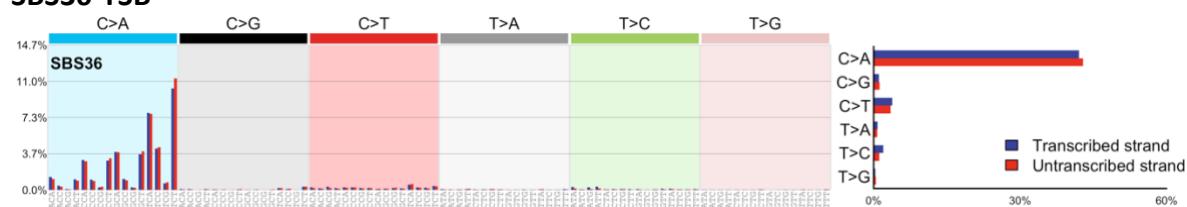
Comments

SBS35 exhibits a pattern of mutations that encompasses SBS31 and both may be due to platinum drug treatment.

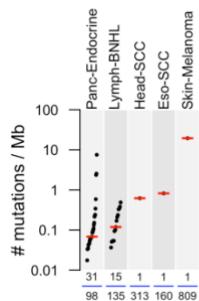
SBS36 (v3.0)



SBS36-TSB



Cancer types in which the signature is found



Proposed aetiology

Defective base excision repair, including DNA damage due to reactive oxygen species, due to biallelic germline or somatic *MUTYH* mutations.

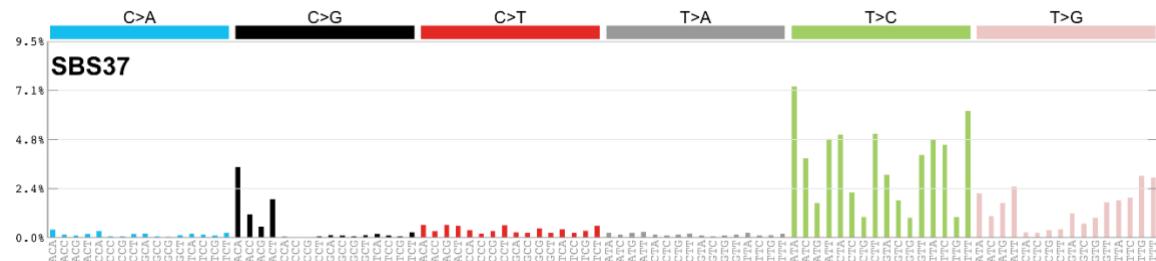
Associated mutation classes and signatures

N/A

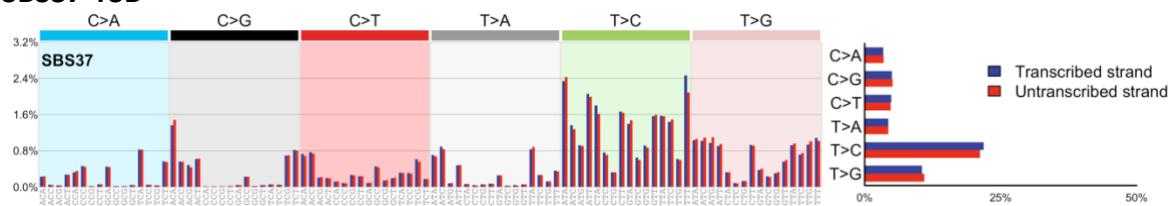
Comments

Similar to SBS18, which has been proposed to be due to reactive oxygen species induced DNA damage.

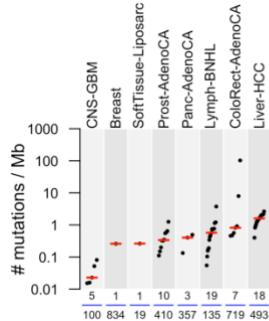
SBS37 (v3.0)



SBS37-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown.

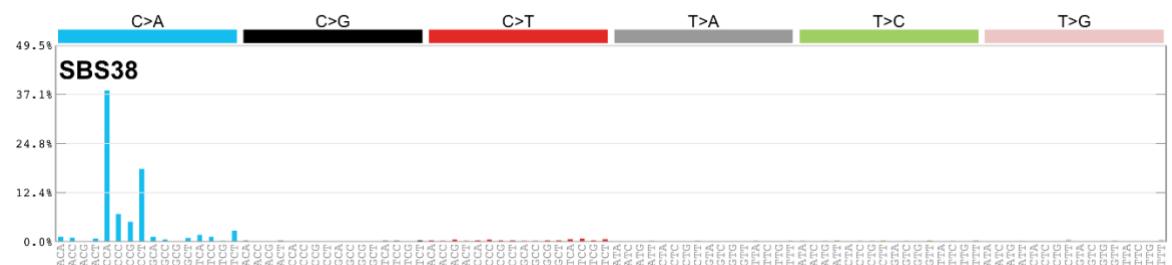
Associated mutation classes and signatures

N/A

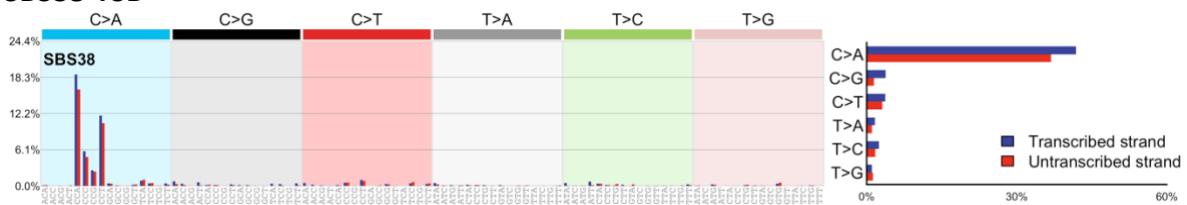
Comments

N/A

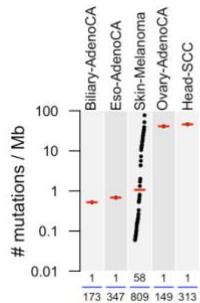
SBS38 (v3.0)



SBS38-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown. Found only in ultraviolet light associated melanomas suggesting potential indirect damage from UV-light.

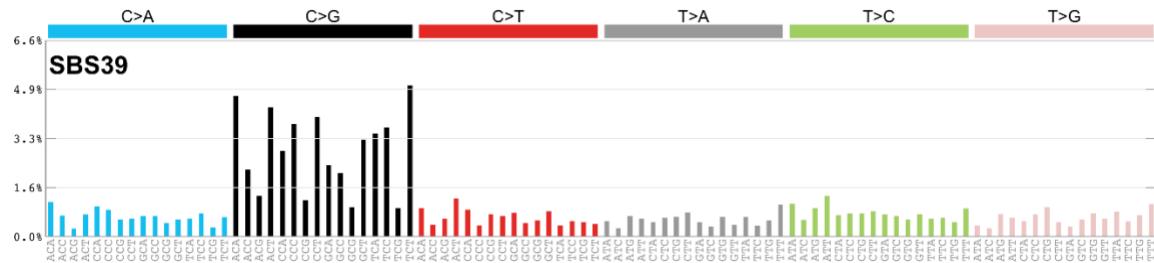
Associated mutation classes and signatures

N/A

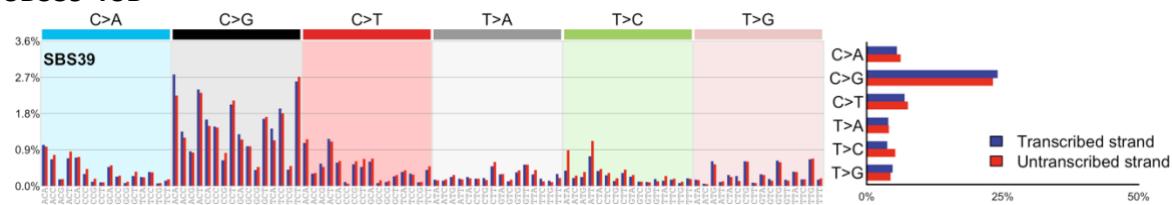
Comments

N/A

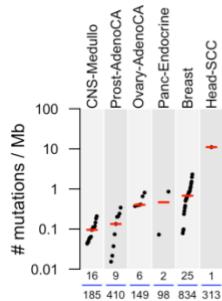
SBS39 (v3.0)



SBS39-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown.

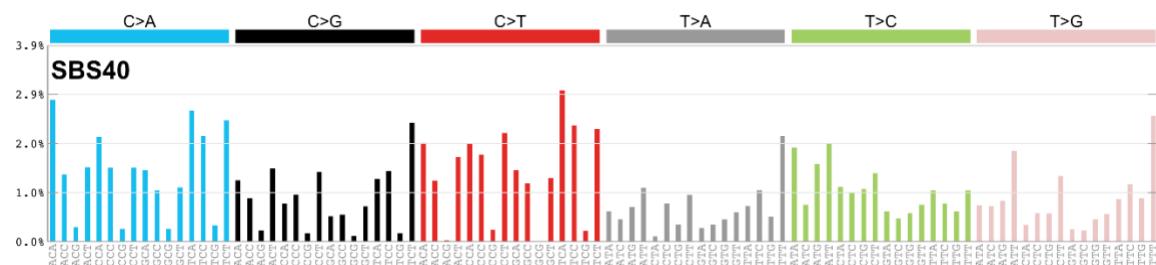
Associated mutation classes and signatures

N/A

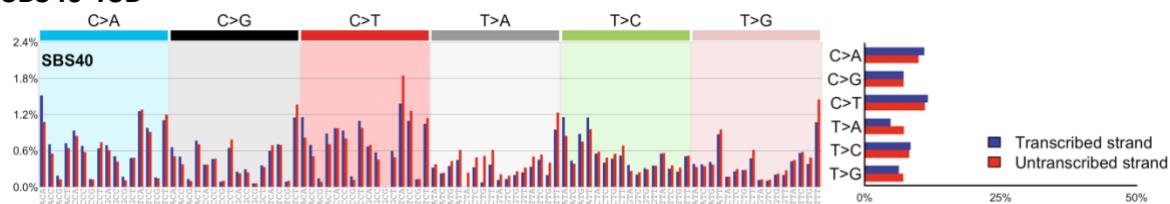
Comments

N/A

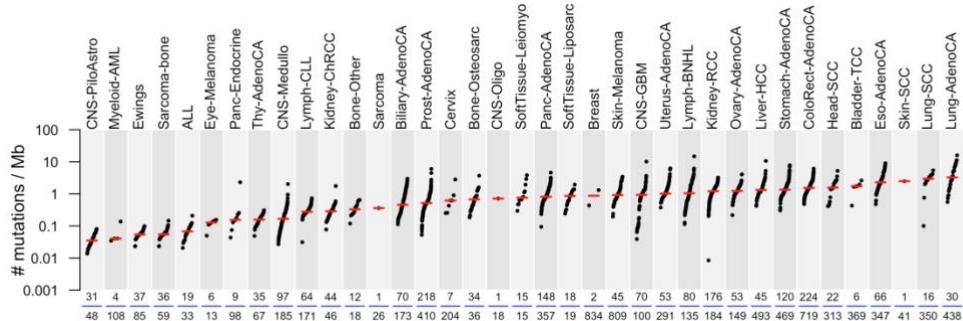
SBS40 (v3.0)



SBS40-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown.

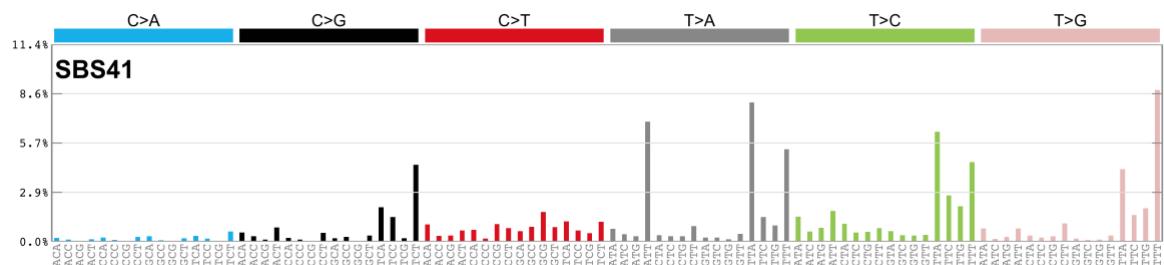
Associated mutation classes and signatures

N/A

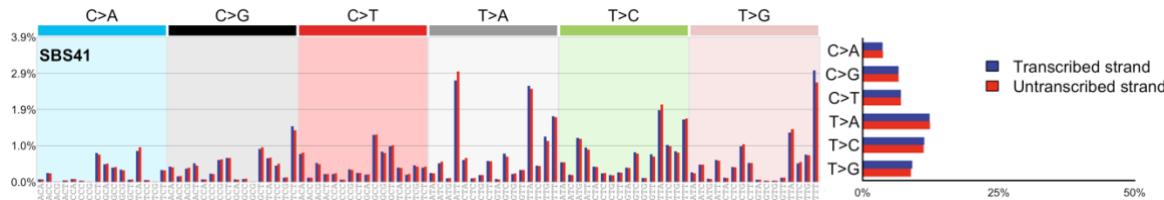
Comments

Numbers of mutations attributed to SBS40 are correlated with patients' ages for some types of human cancer.

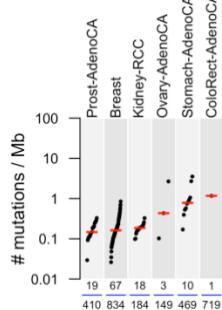
SBS41 (v3.0)



SBS41-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown

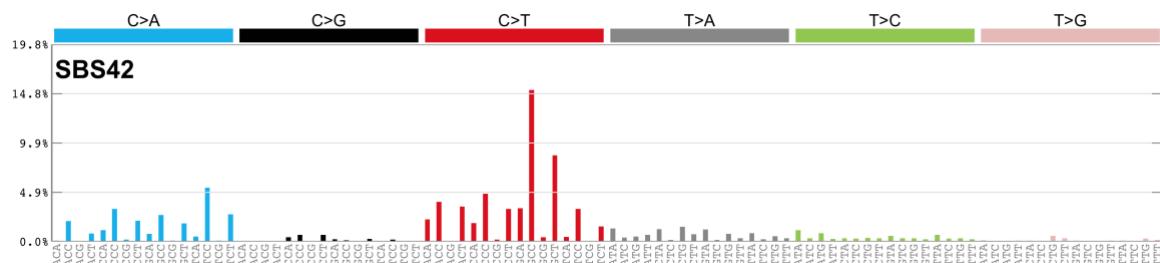
Associated mutation classes and signatures

N/A

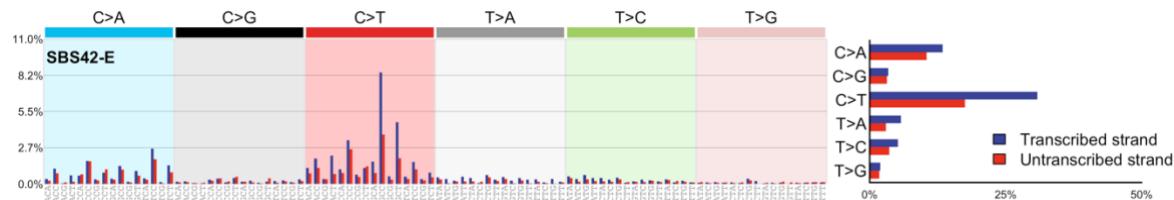
Comments

N/A

SBS42 (v3.0)

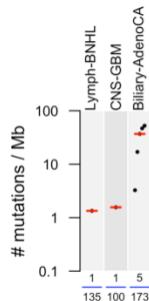


SBS42-TSB



Transcriptional strand bias of C>A mutations with more G than C mutations on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair. Transcriptional strand bias of C>T mutations with more G than C mutations on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair. Please note that SBS42 has only been found in exome sequencing data and, as such, the transcriptional strand bias reflects the one observed in the coding regions of the genome.

Cancer types in which the signature is found



Proposed aetiology

Occupational exposure to haloalkanes.

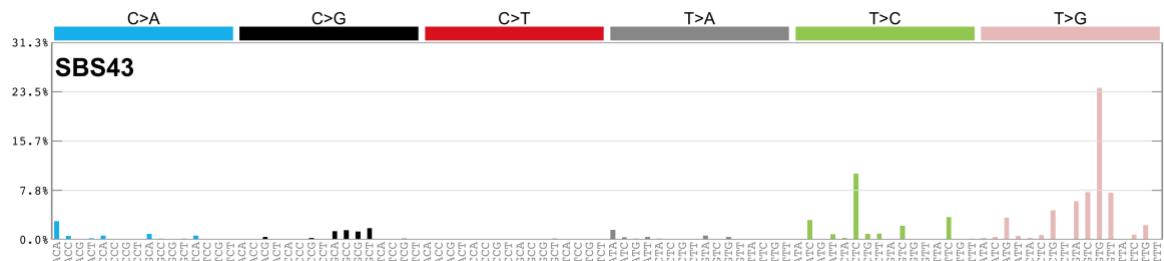
Associated mutation classes and signatures

N/A

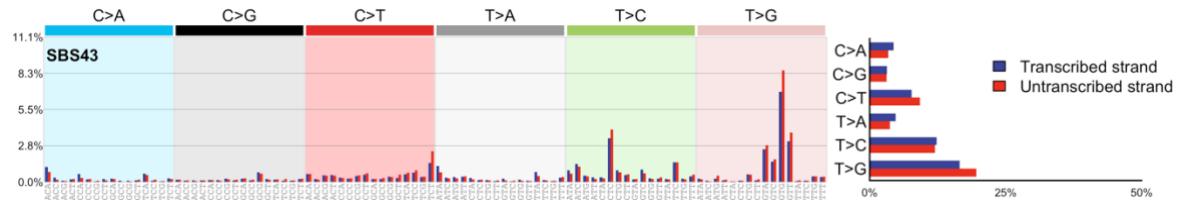
Comments

N/A

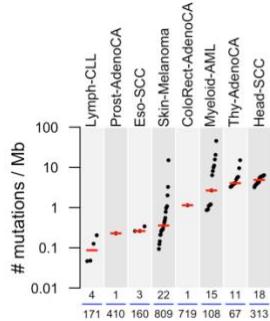
SBS43 (v3.0)



SBS43-TSB



Cancer types in which the signature is found



Proposed aetiology

Unknown. Possible sequencing artefact.

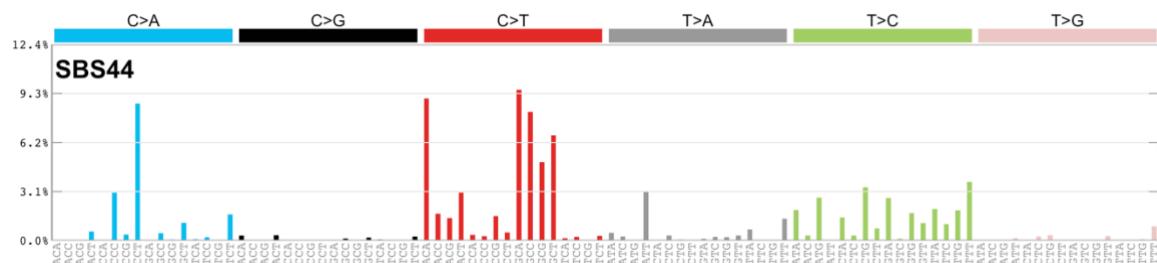
Associated mutation classes and signatures

N/A

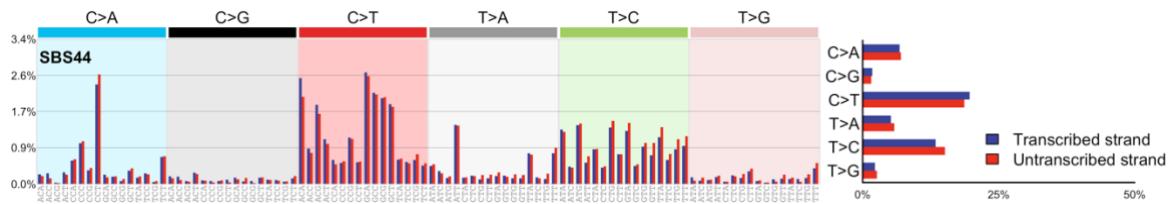
Comments

N/A

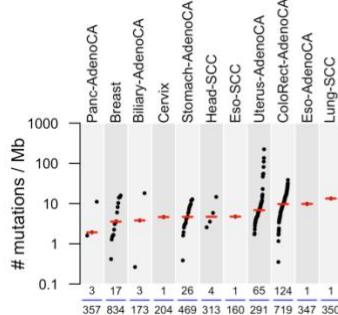
SBS44



SBS44-TSB



Cancer types in which the signature is found



Proposed aetiology

Defective DNA mismatch repair.

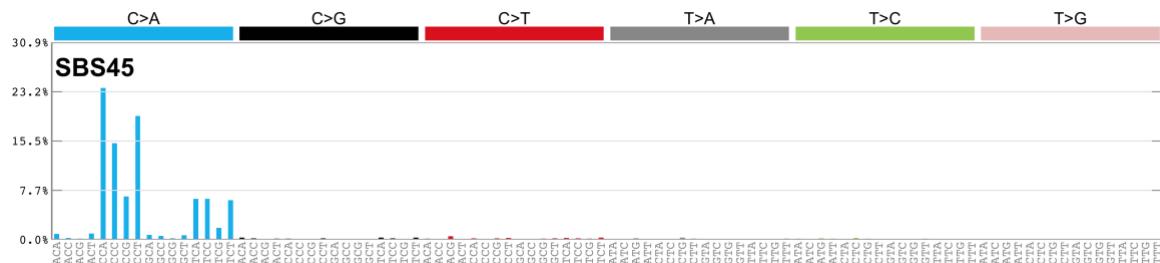
Associated mutation classes and signatures

SBS44 is associated with ID1 and ID2.

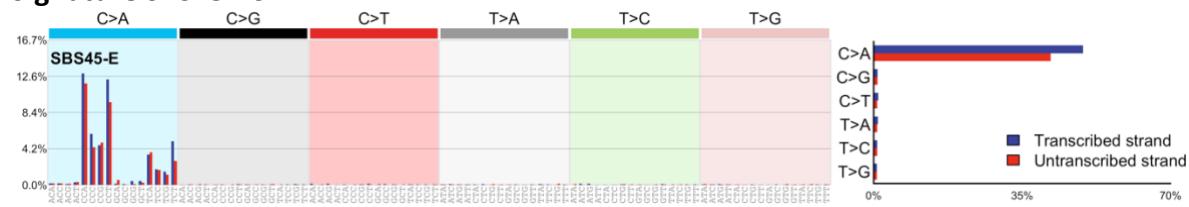
Comments

SBS44 is one of seven mutational signatures associated with defective DNA mismatch repair (MSI) and is often found in the same samples as other MSI associated signatures: SBS6, SBS14, SBS15, SBS20, SBS21, and SBS26.

SBS45 (v3.0)

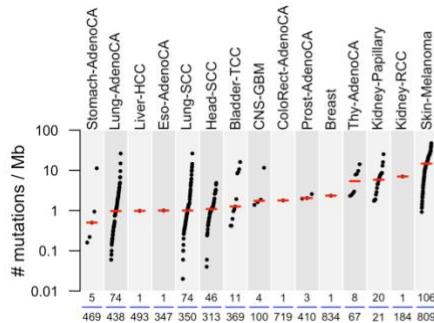


Signature SBS45-TSB



Weak transcriptional strand bias of C>A mutations with more G than C mutations on the untranscribed strands of genes consistent with damage to guanine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Possible artefact due to 8-oxo-guanine introduced during sequencing.

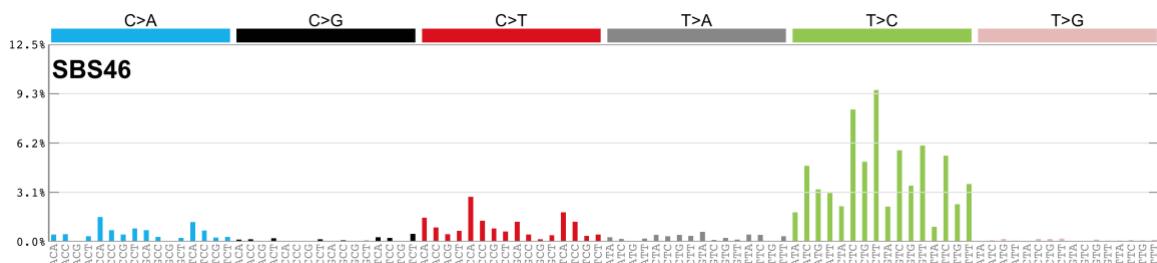
Associated mutation classes and signatures

N/A

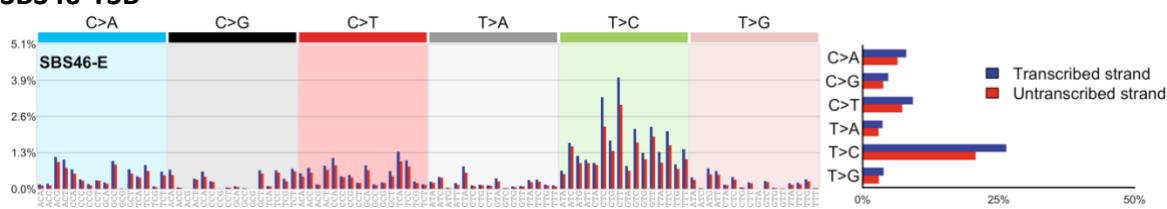
Comments

N/A

SBS46

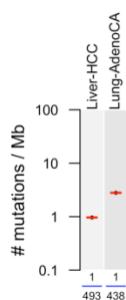


SBS46-TSB



Transcriptional strand-bias for T>C substitutions with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription-coupled nucleotide excision repair. Please note that signature SBS46 has only been found in exome sequencing data and, as such, the transcriptional strand bias reflects the one observed in the coding regions of the genome.

Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

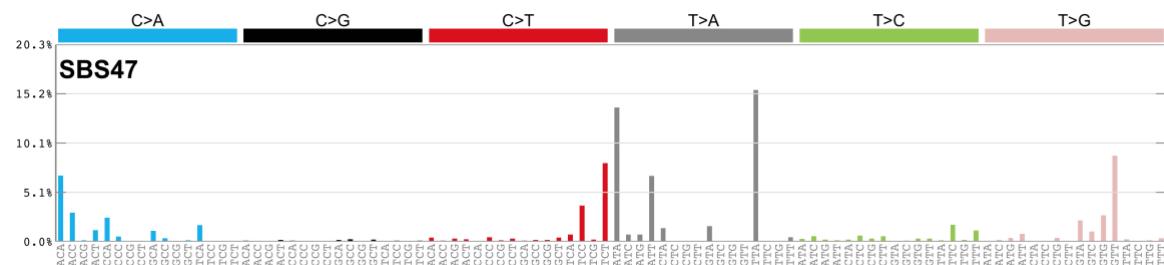
Associated mutation classes and signatures

N/A

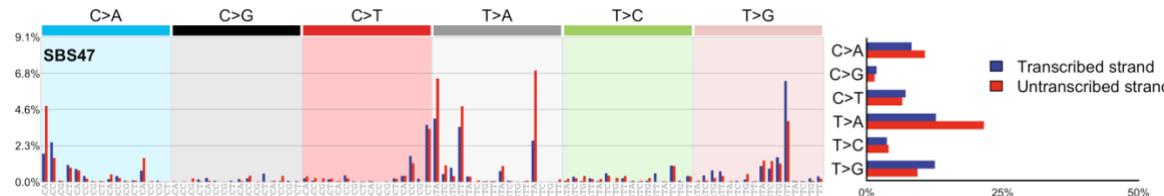
Comments

Signature SBS46 was found commonly in colorectal cancers from early releases of TCGA (data released prior 2013).

SBS47 (v3.0)



SBS47-TSB



SBS47 exhibits inconsistent transcriptional strand bias. Transcriptional strand-bias for T>A substitutions with more mutations of T than A on the untranscribed strands of genes consistent with damage to thymine and repair by transcription-coupled nucleotide excision repair. Transcriptional strand-bias for T>G substitutions with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found

N/A

Proposed aetiology

Possible sequencing artefact.

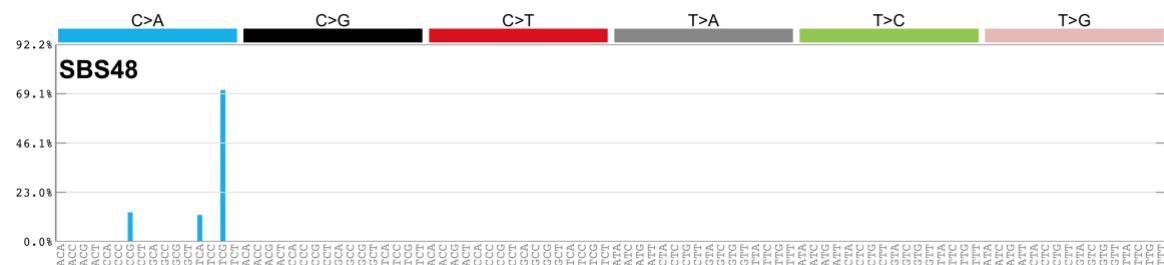
Associated mutation classes and signatures

N/A

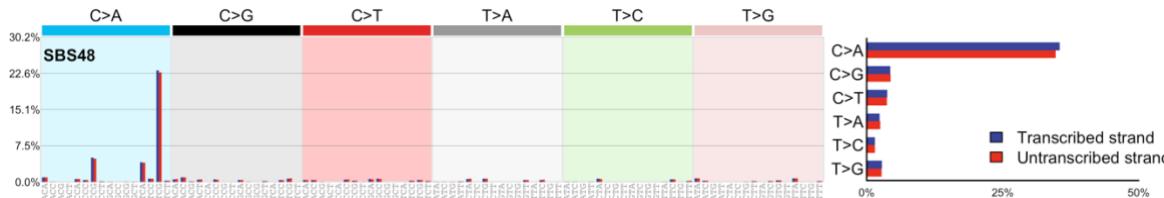
Comments

SBS47 was found in cancer samples that were subsequently blacklisted for poor quality of sequencing data.

SBS48 (v3.0)



SBS48-TSB



Cancer types in which the signature is found

N/A

Proposed aetiology

Possible sequencing artefact.

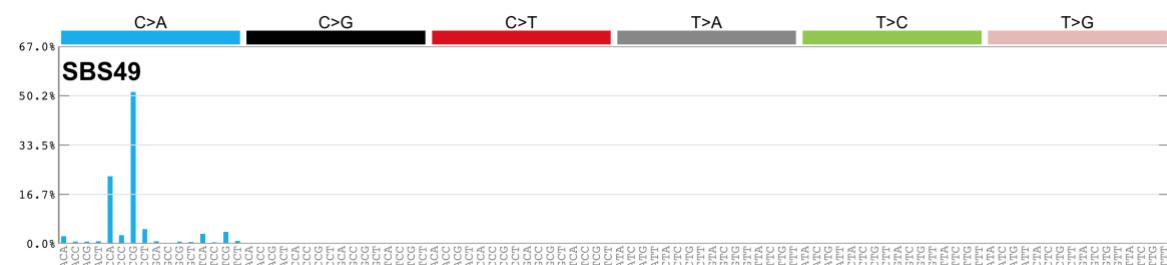
Associated mutation classes and signatures

N/A

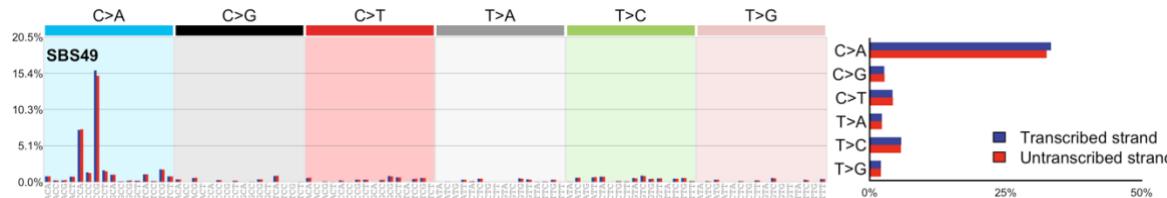
Comments

SBS48 was found in cancer samples that were subsequently blacklisted for poor quality of sequencing data.

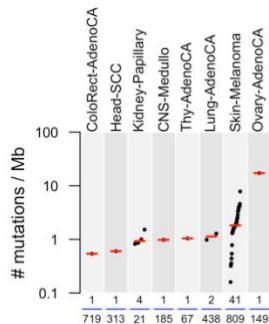
SBS49 (v3.0)



SBS49-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

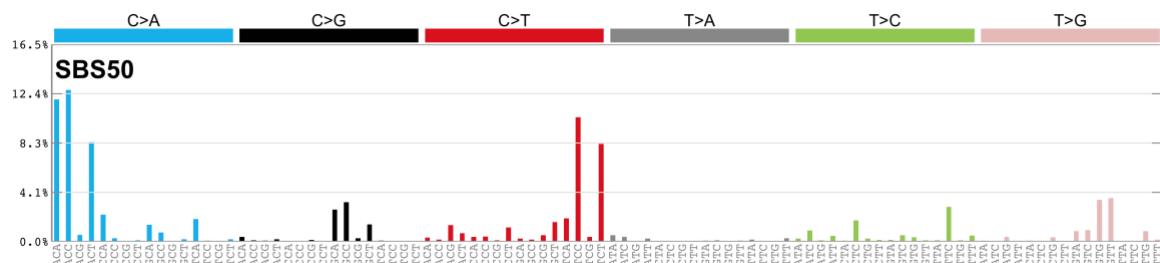
Associated mutation classes and signatures

N/A

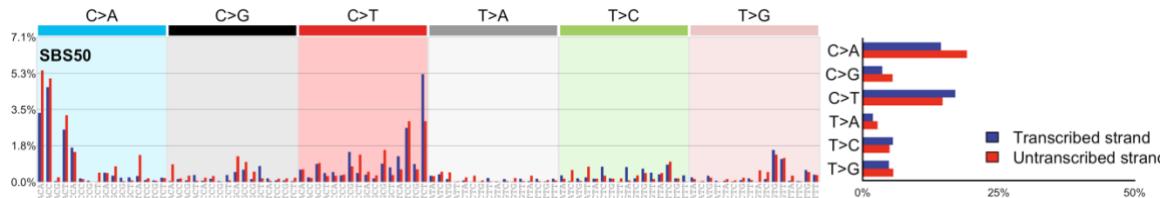
Comments

N/A

SBS50 (v3.0)

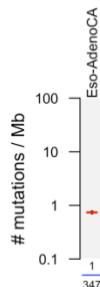


SBS50-TSB



Signature SBS50 exhibits transcriptional strand-bias for C>A substitutions with more mutations of C than G on the untranscribed strands of genes consistent with damage to cytosine and repair by transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

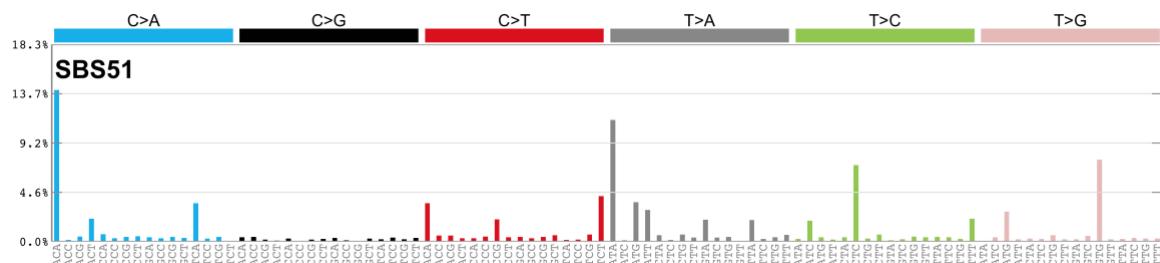
Associated mutation classes and signatures

N/A

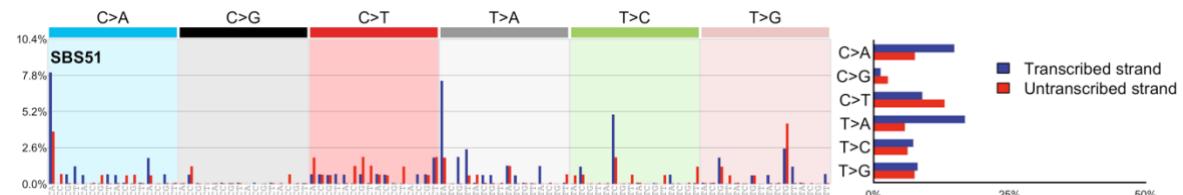
Comments

SBS50 was found in cancer samples that were subsequently blacklisted for poor quality of sequencing data.

SBS51 (v3.0)

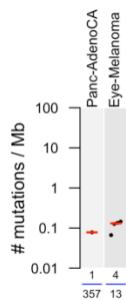


SBS51-TSB



Signature SBS51 exhibits inconsistent transcriptional strand bias. Transcriptional strand-bias for C>A substitutions with more mutations of G than C on the untranscribed strands of genes consistent with damage to guanine and repair by transcription-coupled nucleotide excision repair. Transcriptional strand-bias for C>T substitutions with more mutations of C than G on the untranscribed strands of genes consistent with damage to cytosine and repair by transcription-coupled nucleotide excision repair. Transcriptional strand-bias for T>A substitutions with more mutations of A than T on the untranscribed strands of genes consistent with damage to adenine and repair by transcription-coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

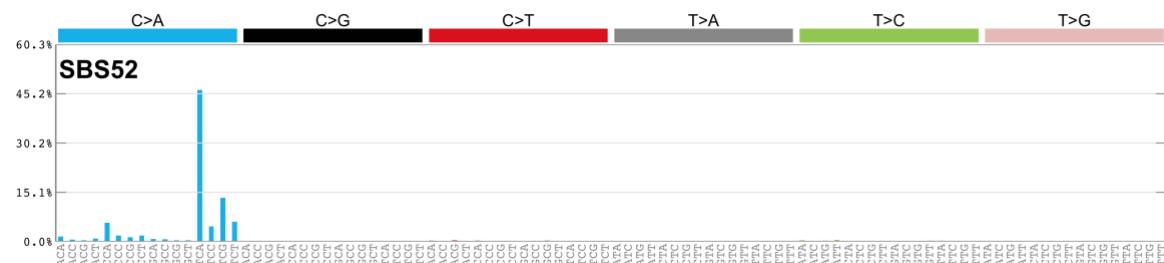
Associated mutation classes and signatures

N/A

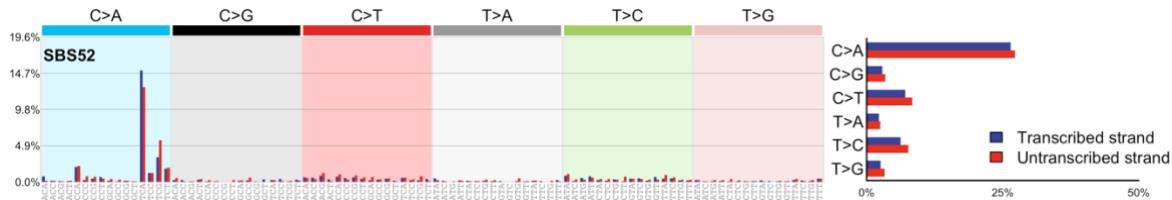
Comments

N/A

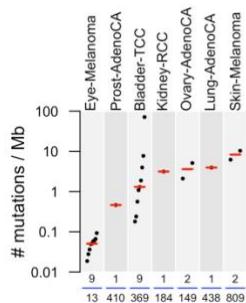
SBS52 (v3.0)



SBS52-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

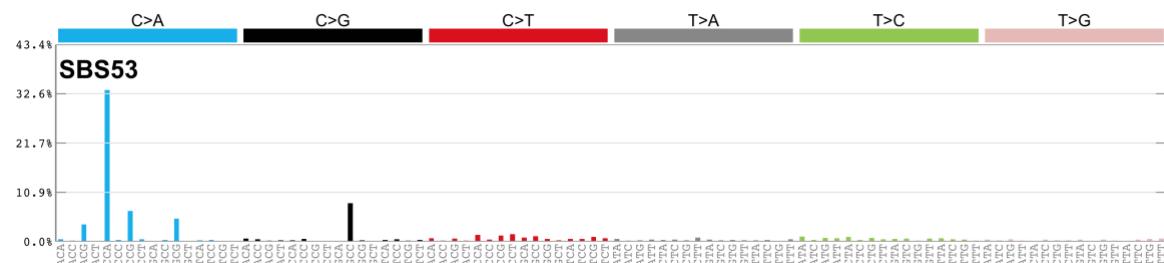
Associated mutation classes and signatures

N/A

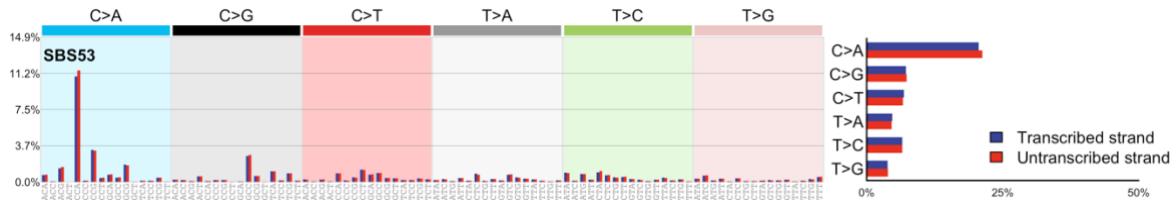
Comments

N/A

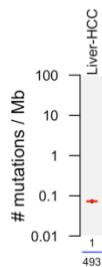
SBS53 (v3.0)



SBS53-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

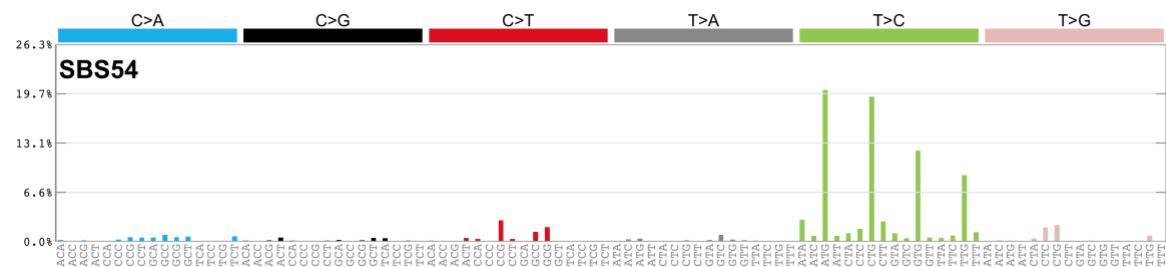
Associated mutation classes and signatures

N/A

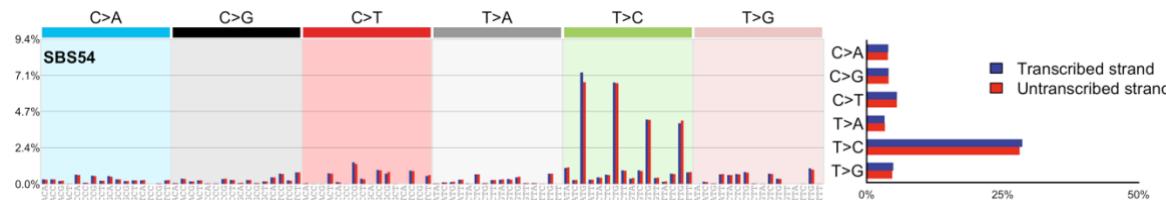
Comments

Signature SBS53 was found in cancer samples that were subsequently blacklisted for poor quality of sequencing data.

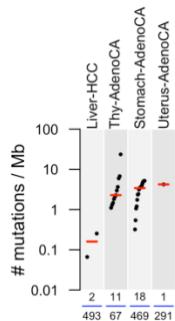
SBS54 (v3.0)



SBS54-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact. Possible contamination with germline variants.

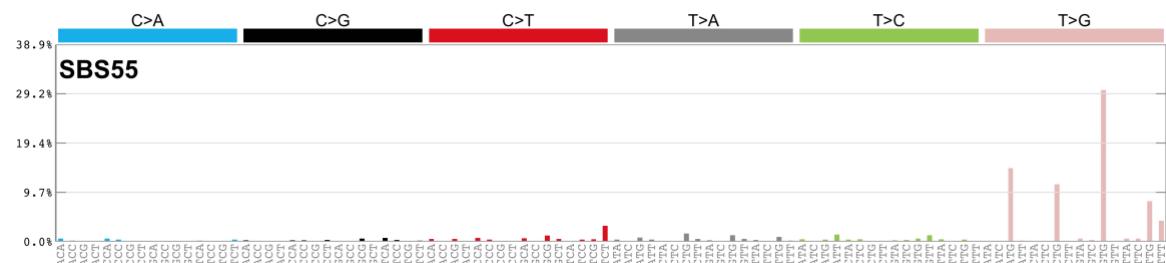
Associated mutation classes and signatures

N/A

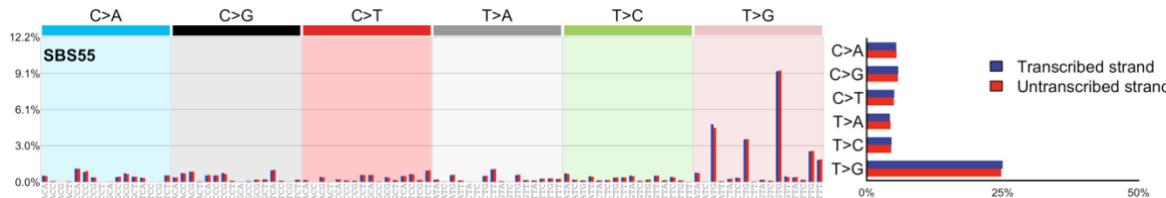
Comments

N/A

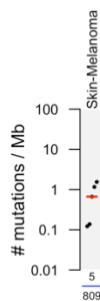
SBS55 (v3.0)



SBS55-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

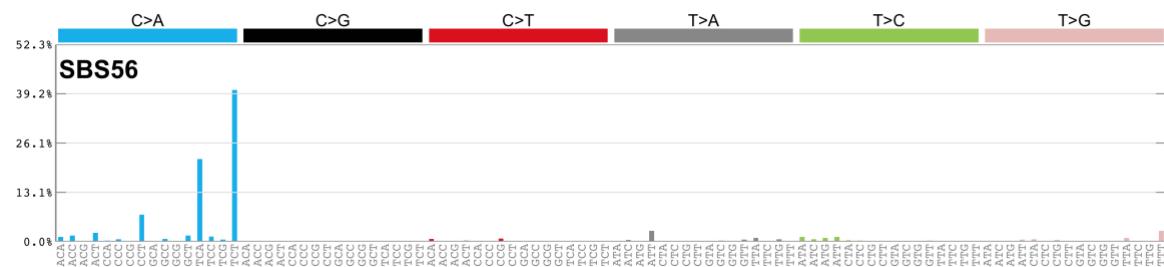
Associated mutation classes and signatures

N/A

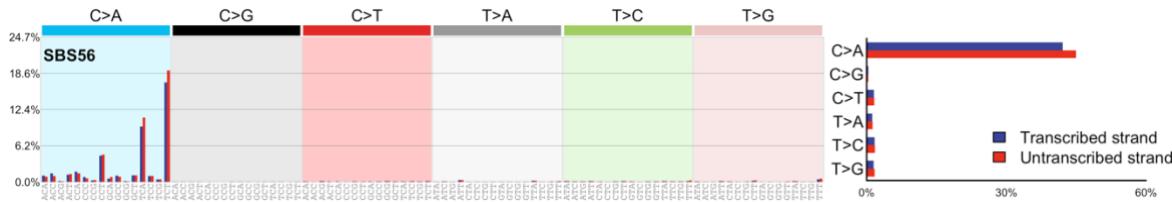
Comments

N/A

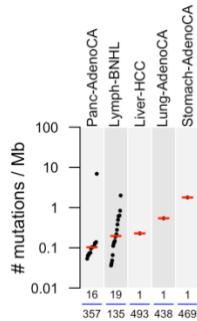
SBS56 (v3.0)



SBS56-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

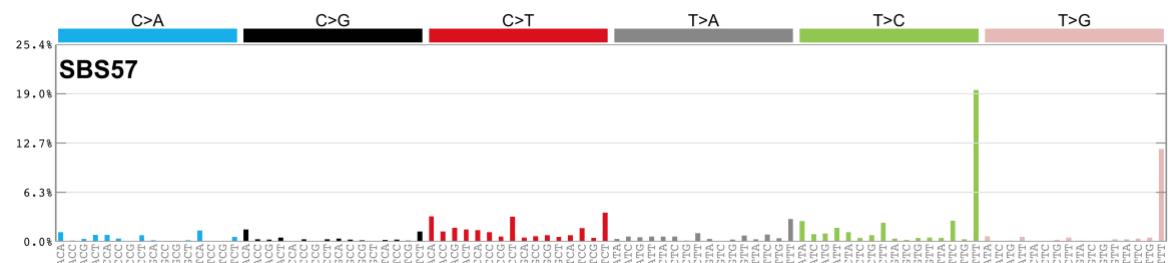
Associated mutation classes and signatures

N/A

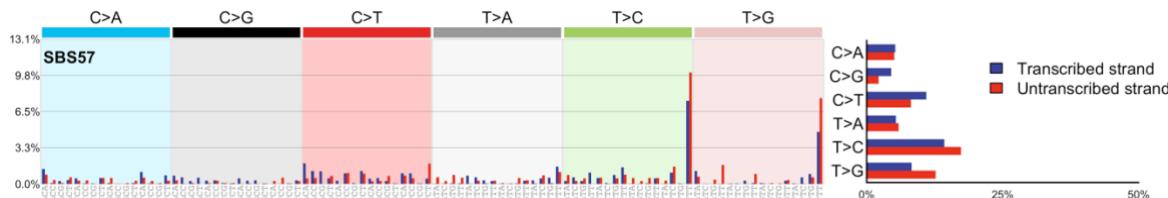
Comments

N/A

SBS57 (v3.0)

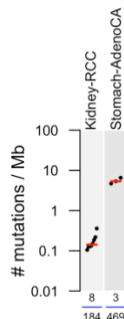


SBS57-TSB



Transcriptional strand bias of T>C and T>G mutations with more T than A mutations on the untranscribed strands of genes consistent with damage to thymine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

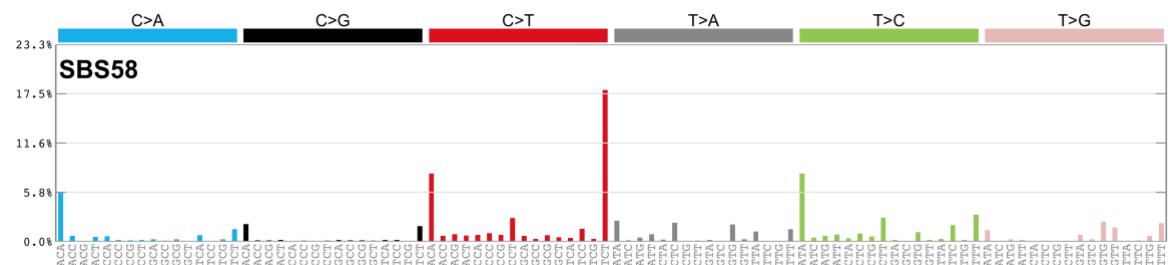
Associated mutation classes and signatures

N/A

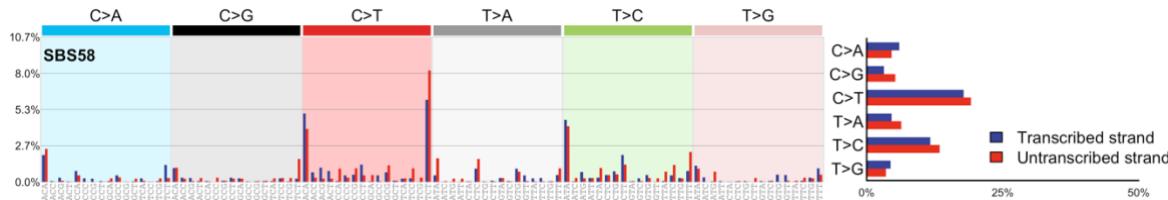
Comments

N/A

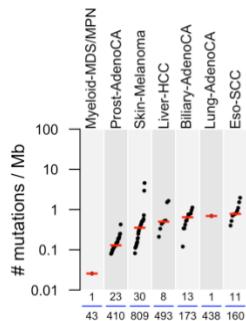
SBS58 (v3.0)



SBS58-TSB



Cancer types in which the signature is found



Proposed aetiology

Potential sequencing artefact.

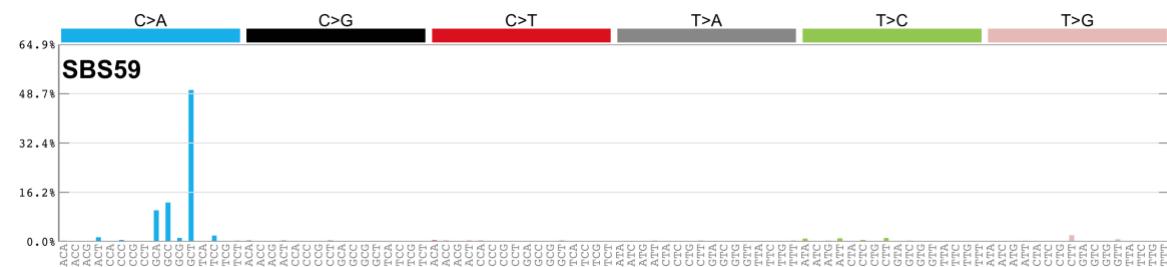
Associated mutation classes and signatures

N/A

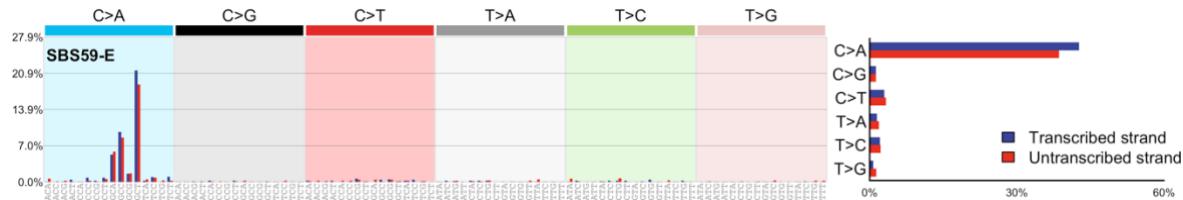
Comments

N/A

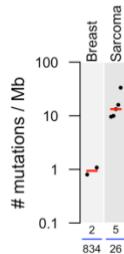
SBS59 (v3.0)



SBS59-TSB



Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

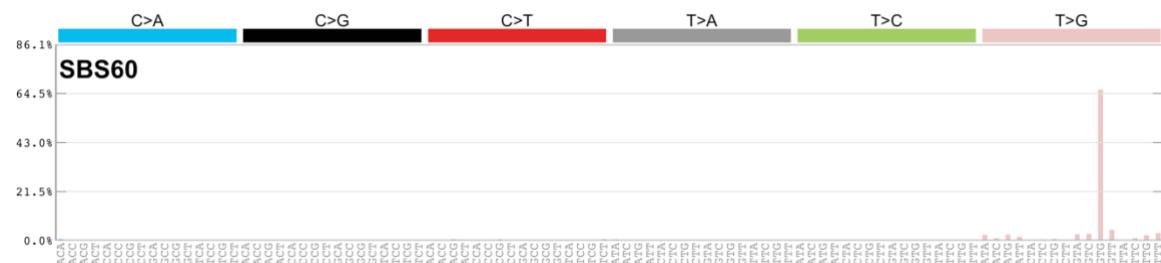
Associated mutation classes and signatures

N/A

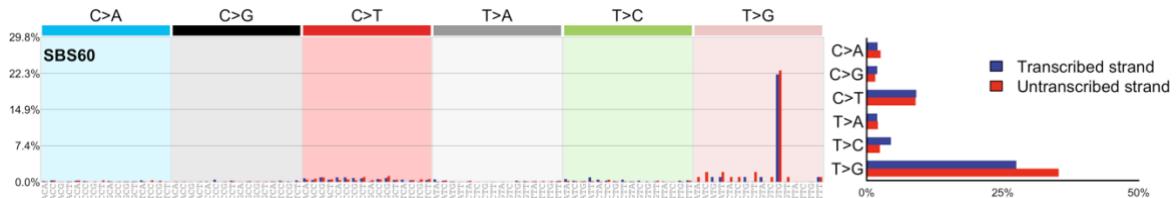
Comments

N/A

SBS60

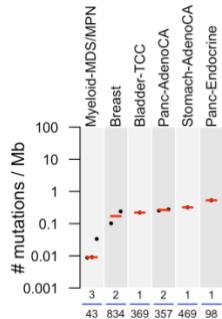


SBS60-TSB



Transcriptional strand bias of T>G mutations with more T than A mutations on the untranscribed strands of genes consistent with damage to thymine and repair by transcription coupled nucleotide excision repair.

Cancer types in which the signature is found



Proposed aetiology

Possible sequencing artefact.

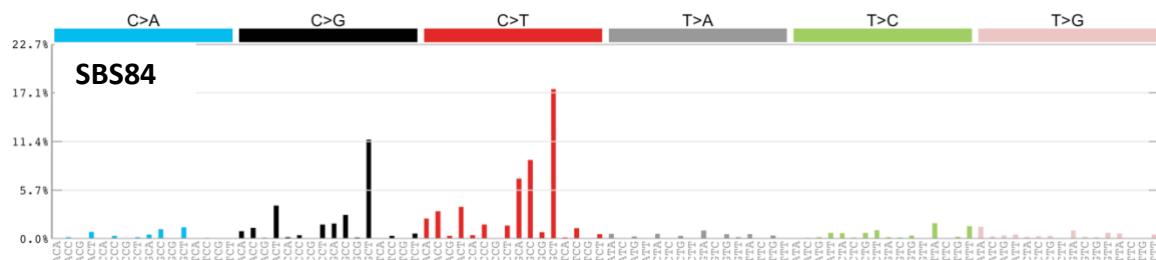
Associated mutation classes and signatures

N/A

Comments

N/A

SBS84



SBS84-TSB

(Not available.)

Cancer types in which the signature is found

Cancers of lymphoid origin.

Proposed aetiology

Activity of activation-induced cytidine deaminase (AID).

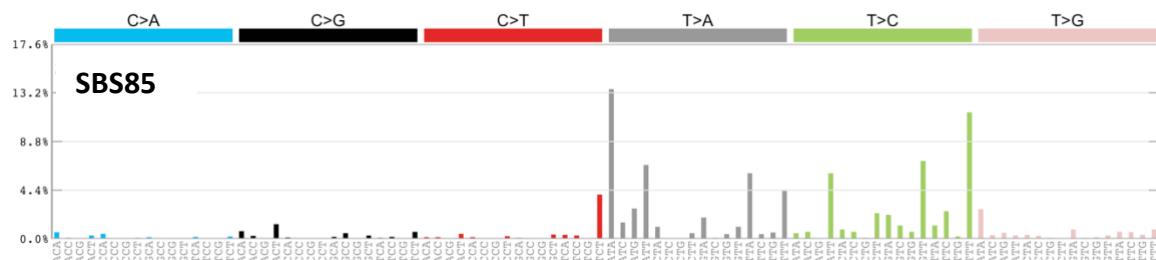
Associated mutation classes and signatures

Associated with SBS85.

Comments

SBS84 is found in clustered mutations in the immunoglobulin gene and other regions in lymphoid cancers.

SBS85



SBS85-TSB

(Not available)

Cancer types in which the signature is found

Cancers of lymphoid origins.

Proposed aetiology

Indirect effects of activation-induced cytidine deaminase (AID) induced somatic mutagenesis in lymphoid cells.

Associated mutation classes and signatures

Associated with SBS84.

Comments

SBS85 is found in clustered mutations in the immunoglobulin gene and other regions in lymphoid cancers.