

## Solid Tumour Section

### Review

# Lung: Translocations in Squamous Cell Carcinoma

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Published in Atlas Database: October 2014

Online updated version : <http://AtlasGeneticsOncology.org/Tumors/TranslocLungSquamCellCarclD6819.html>

Printable original version : <http://documents.irevues.inist.fr/bitstream/handle/2042/62264/10-2014-TranslocLungSquamCellCarclD6819.pdf>  
DOI: 10.4267/2042/62264

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## Abstract

Review on translocations in lung squamous cell carcinoma, with data on clinics, genetics and cytogenetics.

## Classification

In the group of malignant epithelial tumours of the lungs, squamous cell carcinomas belong to the non-small cell carcinomas (non-small cell lung cancer (NSCLC)), as opposed to small cell carcinomas (SCLC). Other NSCLCs are: adenocarcinomas, adenosquamous carcinomas, large cell carcinomas, sarcomatoid carcinomas, carcinoid tumours, salivary gland tumours.

## Clinics and pathology

### Epidemiology

Squamous cell carcinoma is the most frequent lung cancer in male patients, representing about 40% of the cases, and only 25% in women (much less frequent in female patients than adenocarcinoma). Squamous cell carcinoma is the lung cancer the most often associated with tobacco smoking. Location of the tumour is usually central, present as a perihilar mass, with or without lobar collapse and obstructive pneumonitis, but it can also be peripheral at times.

### Pathology

There are small cell variants (differential diagnosis: SCLC), clear cell variants, well-differentiated papillary variants, basaloid variants with a very aggressive clinical course, and spindle cell

(sarcomatoid) carcinosarcoma variants of the typical squamous cell carcinoma.

The expression of cytokeratins (CK) CK5/6, CK34BE12 and TP63 (3q28, also called P63) are strong in squamous cell carcinoma, whereas the expression of CK7 and NKX2-1 (14q13, also called TTF-1) are strong in adenocarcinoma (Xu et al., 2014).

### Evolution

Staging is performed according to the TNM system.

## Genetics

### Note

TP53 (17p13) mutations are detected in most cases. In a large recent study, altered pathways included NFE2L2/KEAP1 in 34%, squamous differentiation genes in 44%, PI3K/AKT in 47%, and CDKN2A/RB1 in 72% of tumors. In contrast to what is found in adenocarcinoma, mutations in EGFR (7p11) or in KRAS (12p12) are extremely rare in squamous cell carcinoma of the lungs (Cancer Genome Atlas Research Network, 2012). DDR2 (1q23) is inactivated in about 4% of cases; FGFR1 (8p11) and FGFR3 (4p16) are amplified in 5 to 10% of cases (Majewski et al., 2013; Seo et al., 2014).

## Cytogenetics

### Note

Of 157 translocations so far reported in squamous cell carcinoma of the lungs, 1 gene was found five times implicated: ATP11B (3q26, which catalyzes the hydrolysis of ATP); 1 gene was implicated in three different translocations: MCF2L2 (3q27, a

guanine nucleotide exchange factor); and 13 genes were found twice: ANGPT1 (8q23), EIF4EBP1 (8p11), EML4 (2p21), IGF2 (11p15), ITSN1 (21q22), KLHL29 (2p24), MAN1A2 (1p13), MGAT5 (2q21), NPAS3 (14q13), PPP6R3 (14q13), ROS1 (6q22), TMCC1 (3q22), and TTC28 (22q12). Finally, 280 genes were found implicated in one translocation.

### **Cytogenetics Morphological**

The translocations are the following:

t(1;1)(p36;p36) PRKCZ/SKI (Majewski et al., 2013)  
 t(1;1)(p34;q44) SMYD3/ELOVL1 (Cancer Genome Atlas Research Network, 2012)  
 t(1;1)(q21;q21) GATAD2B/PRKAB2 (Cancer Genome Atlas Research Network, 2012)  
 t(1;2)(p35;q37) ZBTB8B/TRAF3IP1 (Cancer Genome Atlas Research Network, 2012)  
 t(1;2)(p12;p16) REL/MAN1A2 (Cancer Genome Atlas Research Network, 2012)  
 t(1;2)(p12;p15) PHGDH/WDPCP (Cancer Genome Atlas Research Network, 2012)  
 t(1;3)(p34;q26) ATP11B/POU3F1 (Cancer Genome Atlas Research Network, 2012)  
 t(1;3)(p34;q26) OSCP1/SOX2-OT (Cancer Genome Atlas Research Network, 2012)  
 t(1;3)(p33;q29) TFRC/NSUN4 (Cancer Genome Atlas Research Network, 2012)  
 t(1;4)(p31;q22) BMPR1B/ALG6 (Cancer Genome Atlas Research Network, 2012)  
 t(1;5)(p34;q31) CTNNA1/HEYL (Cancer Genome Atlas Research Network, 2012)  
 t(1;5)(q25;p13) DARS2/ZFR (Cancer Genome Atlas Research Network, 2012)  
 t(1;8)(p36;q21) SLC7A13/WDTC1 (Cancer Genome Atlas Research Network, 2012)  
 t(1;8)(p32;q24) NRD1/KCNK9 (Cancer Genome Atlas Research Network, 2012)  
 t(1;9)(p33;p13) KIF24/FAAH (Cancer Genome Atlas Research Network, 2012)  
 t(1;10)(p32;q21) CDK1/USP24 (Cancer Genome Atlas Research Network, 2012)  
 t(1;10)(p31;p14) SFMBT2/PRKACB (Cancer Genome Atlas Research Network, 2012)  
 t(1;10)(q32;q22) TMEM206/PSAP (Cancer Genome Atlas Research Network, 2012)  
 t(1;11)(p31;q24) ETS1/NEGR1 (Cancer Genome Atlas Research Network, 2012)  
 t(1;12)(q25;p12) HMCN1/ETNK1 (Cancer Genome Atlas Research Network, 2012)  
 t(1;16)(q21;p12) CCP110/GOLPH3L (Cancer Genome Atlas Research Network, 2012)  
 t(1;17)(p21;q25) UNK/DPYD (Cancer Genome Atlas Research Network, 2012)  
 t(1;17)(p12;q11) ALDOC/MAN1A2 (Cancer Genome Atlas Research Network, 2012)  
 t(1;21)(p35;q22) ITSN1/MATN1 (Cancer Genome Atlas Research Network, 2012)

t(2;2)(p25;p25) ROCK2/SH3YL1 (Cancer Genome Atlas Research Network, 2012)  
 t(2;2)(p24;p23) GPN1/KLHL29 (Cancer Genome Atlas Research Network, 2012)  
 inv(2)(p21p23) or del(2)(p21p23) EML4/ALK (Rikova et al., 2007; Soda et al., 2007; Martelli et al., 2009)  
 t(2;2)(p21;p21) THADA/EML4 (Cancer Genome Atlas Research Network, 2012)  
 t(2;2)(p16;p23) PSME4/PPP1CB (Cancer Genome Atlas Research Network, 2012)  
 t(2;2)(p15;p15) EHBP1/FAM161A (Cancer Genome Atlas Research Network, 2012)  
 t(2;2)(q21;q21) GPR39/MGAT5 (Cancer Genome Atlas Research Network, 2012)  
 t(2;2)(q21;q24) ACVR1C/MGAT5 (Cancer Genome Atlas Research Network, 2012)  
 t(2;2)(q23;q35) TNS1/RPRM (Cancer Genome Atlas Research Network, 2012)  
 t(2;3)(p16;q26) KCNMB2/NRXN1 (Cancer Genome Atlas Research Network, 2012)  
 t(2;4)(p16;q13) BCL11A/EPHA5 (Cancer Genome Atlas Research Network, 2012)  
 t(2;5)(p16;p15) NRXN1/PLEKHG4B (Cancer Genome Atlas Research Network, 2012)  
 t(2;5)(p11;p12) HCN1/FUNDC2P2 (Cancer Genome Atlas Research Network, 2012)  
 t(2;5)(q35;p13) USP37/OSMR (Cancer Genome Atlas Research Network, 2012)  
 t(2;6)(p24;p22) ID4/FAM84A (Cancer Genome Atlas Research Network, 2012)  
 t(2;16)(q24;q11) ANKRD26P1/SLC4A10 (Cancer Genome Atlas Research Network, 2012)  
 t(2;17)(p25;q21) CRHR1-IT1/ALLC (Cancer Genome Atlas Research Network, 2012)  
 t(2;18)(p24;q11) KLHL29/PSMA8 (Cancer Genome Atlas Research Network, 2012)  
 t(2;22)(p12;q12) EVA1A/TTC28 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(p12;q29) PAK2/VGLL3 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q11;q13) ALCAM/EPHA6 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q12;q13) GSK3B/IMPG2 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q13;q22) SLCO2A1/GUCA1C (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q21;q22) RUVBL1/TMCC1 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q22;q22) PIK3CB/BFSP2 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q22;q22) TMCC1/C3orf36 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q24;q26) HLTF/OTOL1 (Cancer Genome Atlas Research Network, 2012)  
 t(3;3)(q25;q25) GMPS/C3orf55 (Cancer Genome Atlas Research Network, 2012)

- t(3;3)(q25;q26) IQCJ/BCHE (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q25;q27) PPM1L/MCF2L2 (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q25;q28) PYDC2/C3orf79 (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q26;q26) ATP11B/SI (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q26;q26) PHC3/FNDC3B (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q26;q27) CCDC39/MCF2L2 (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q26;q28) SOX2/TPRG1 (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q27;q28) LPP/ST6GAL1 (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q27;q29) EHHADH/SENTP5 (Cancer Genome Atlas Research Network, 2012)
- t(3;3)(q29;q29) LRCH3/MIR570 (Cancer Genome Atlas Research Network, 2012)
- t(3;4)(q26;p16) ATP11B/ZNF595 (Cancer Genome Atlas Research Network, 2012)
- t(3;8)(q27;q22) MCF2L2/MIR548A3 (Cancer Genome Atlas Research Network, 2012)
- t(3;8)(q29;p12) FYTDD1/WRN (Cancer Genome Atlas Research Network, 2012)
- t(3;11)(q26;p15) PDE3B/ATP11B (Cancer Genome Atlas Research Network, 2012)
- t(3;13)(q21;q33) TNFSF13B/MYLK (Cancer Genome Atlas Research Network, 2012)
- t(3;17)(q25;p11) MAP2K3/SSR3 (Cancer Genome Atlas Research Network, 2012)
- t(3;17)(q29;q23) MIR21/WDR53 (Cancer Genome Atlas Research Network, 2012)
- t(3;19)(q27;q13) ACTN4/IGF2BP2 (Cancer Genome Atlas Research Network, 2012)
- t(3;20)(q21;q13) SLC12A8/BCAS1 (Cancer Genome Atlas Research Network, 2012)
- t(3;21)(p11;q21) POU1F1/TMPRSS15 (Cancer Genome Atlas Research Network, 2012)
- t(3;22)(q26;q11) ATP11B/TPTEP1 (Cancer Genome Atlas Research Network, 2012)
- del(4)(p16p16) FGFR3/TACC3 (Majewski et al., 2013; Wu et al. 2013)
- t(4;4)(q13;q22) CCSER1/UGT2A1 (Cancer Genome Atlas Research Network, 2012)
- t(4;6)(p15;q22) SLC34A2/ROS1 (Davies et al., 2012)
- t(4;8)(q13;q24) COX18/ZFAT (Cancer Genome Atlas Research Network, 2012)
- t(4;9)(q13;q32) ADAMTS3/SNX30 (Cancer Genome Atlas Research Network, 2012)
- t(4;10)(p13;q11) SGMS1/KCTD8 (Cancer Genome Atlas Research Network, 2012)
- t(5;5)(p15;p15) MARCH6/IRX4 (Cancer Genome Atlas Research Network, 2012)
- t(5;5)(p15;p15) ROPN1L/SEMA5A (Cancer Genome Atlas Research Network, 2012)
- t(5;5)(p12;p13) RICTOR/FGF10 (Cancer Genome Atlas Research Network, 2012)
- t(5;6)(q33;q22) CD74/ROS1 (Davies et al., 2012)
- t(5;8)(p15;q21) MRPS28/ADAMTS16 (Cancer Genome Atlas Research Network, 2012)
- t(5;8)(p13;p11) EIF4EBP1/PRKAA1 (Cancer Genome Atlas Research Network, 2012)
- t(5;11)(q14;q22) FAM151B/CASP12 (Cancer Genome Atlas Research Network, 2012)
- t(5;11)(q35;q14) KCNIP1/KCTD14 (Cancer Genome Atlas Research Network, 2012)
- t(5;12)(p12;q13) NNT/AMIGO2 (Cancer Genome Atlas Research Network, 2012)
- t(6;6)(p25;p25) FAM50B/PPP1R3G (Cancer Genome Atlas Research Network, 2012)
- t(6;6)(p22;q12) EYS/DEK (Cancer Genome Atlas Research Network, 2012)
- t(6;6)(p21;p21) HLA-DOA/MUC21 (Cancer Genome Atlas Research Network, 2012)
- t(6;6)(p12;p22) BEND6/TRIM38 (Cancer Genome Atlas Research Network, 2012)
- t(6;6)(p12;q14) FAM83B/HTR1E (Cancer Genome Atlas Research Network, 2012)
- t(6;6)(q14;q15) GABRR2/ME1 (Cancer Genome Atlas Research Network, 2012)
- t(6;13)(p21;q12) RPL7L1/CDK8 (Cancer Genome Atlas Research Network, 2012)
- t(6;14)(q24;q24) SASH1/DPF3 (Cancer Genome Atlas Research Network, 2012)
- t(6;16)(q13;p13) NTAN1/SLC17A5 (Cancer Genome Atlas Research Network, 2012)
- t(7;7)(p11;p12) VOPP1/GRB10 (Cancer Genome Atlas Research Network, 2012)
- t(7;7)(q22;q31) ANKRD7/DUS4L (Cancer Genome Atlas Research Network, 2012)
- t(7;7)(q31;q33) CHCHD3/MET (Cancer Genome Atlas Research Network, 2012)
- t(7;8)(p14;p23) AMPH/FDFT1 (Majewski et al., 2013)
- t(7;10)(q36;q25) ACTR3C/SORCS1 (Cancer Genome Atlas Research Network, 2012)
- t(8;8)(p11;p11) ADAM9/RNF170 (Cancer Genome Atlas Research Network, 2012)
- t(8;8)(p11;p11) BAG4/FGFR1 (Wu et al., 2013)
- t(8;8)(p11;p11) LETM2/KCNU1 (Cancer Genome Atlas Research Network, 2012)
- t(8;8)(q11;q11) PRKDC/C8orf22 (Cancer Genome Atlas Research Network, 2012)
- t(8;8)(q23;q23) CSMD3/ANGPT1 (Cancer Genome Atlas Research Network, 2012)
- t(8;8)(q23;q23) OXR1/RSPO2 (Cancer Genome Atlas Research Network, 2012)
- t(8;9)(p12;p13) PURG/UBAP1 (Cancer Genome Atlas Research Network, 2012)
- t(8;9)(p11;p21) EIF4EBP1/C9orf53 (Cancer Genome Atlas Research Network, 2012)
- t(8;10)(p21;q26) FGFR2/KIAA1967 (Wu et al., 2013)

t(8;10)(q23;q11) ANGPT1/CXCL12 (Cancer Genome Atlas Research Network, 2012)  
 t(8;11)(q21;p15) HTATIP2/CA1 (Cancer Genome Atlas Research Network, 2012)  
 t(8;15)(q21;q21) NEDD4/RDH10 (Cancer Genome Atlas Research Network, 2012)  
 t(8;16)(p11;p12) KIAA0556/LSM1 (Cancer Genome Atlas Research Network, 2012)  
 t(8;16)(q22;q24) GSE1/NACAP1 (Cancer Genome Atlas Research Network, 2012)  
 t(8;21)(q11;q21) UBE2V2/NRIP1 (Cancer Genome Atlas Research Network, 2012)  
 t(9;9)(p21;p21) CDKN2A/FOCAD (Cancer Genome Atlas Research Network, 2012)  
 t(9;9)(p21;p13) PLAA/RUSC2 (Cancer Genome Atlas Research Network, 2012)  
 t(9;19)(p13;p13) FAM219A/S1PR5 (Cancer Genome Atlas Research Network, 2012)  
 inv(10)(p11q11) KIF5B/RET (Cai et al., 2013)  
 t(10;11)(q21;p15) CTNNA3/IGF2 (Cancer Genome Atlas Research Network, 2012)  
 t(10;11)(q22;q14) P4HA1/TRIM77P (Cancer Genome Atlas Research Network, 2012)  
 t(10;17)(q22;q12) SAMD8/LHX1 (Cancer Genome Atlas Research Network, 2012)  
 t(10;20)(q23;q13) WAPAL/PTPRT (Cancer Genome Atlas Research Network, 2012)  
 t(11;11)(p14;p13) EIF3M/MPPED2 (Cancer Genome Atlas Research Network, 2012)  
 t(11;11)(p11;q12) OR9Q1/OR4C46 (Cancer Genome Atlas Research Network, 2012)  
 t(11;11)(q12;q12) P2RX3/RTN4RL2 (Majewski et al., 2013)  
 t(11;11)(q12;q13) EEF1G/PPP6R3 (Cancer Genome Atlas Research Network, 2012)  
 t(11;11)(q12;q13) SHANK2/MS4A8B (Cancer Genome Atlas Research Network, 2012)  
 t(11;11)(q13;q22) PPP6R3/CNTN5 (Cancer Genome Atlas Research Network, 2012)  
 t(11;12)(p11;p13) ERC1/SPI1 (Cancer Genome Atlas Research Network, 2012)  
 t(12;20)(q12;q13) TAF4/ALG10B (Cancer Genome Atlas Research Network, 2012)  
 t(12;22)(q14;q12) SLC16A7/TTC28 (Cancer Genome Atlas Research Network, 2012)  
 t(13;20)(q12;p12) MACROD2/MPHOSPH8 (Cancer Genome Atlas Research Network, 2012)  
 t(14;14)(q11;q13) NPAS3/OXA1L (Cancer Genome Atlas Research Network, 2012)  
 t(14;14)(q12;q13) FOXP1/NPAS3 (Cancer Genome Atlas Research Network, 2012)  
 t(14;14)(q13;q21) MBIP/C14orf183 (Cancer Genome Atlas Research Network, 2012)  
 t(14;14)(q13;q21) SEC23A/IGBP1P1 (Cancer Genome Atlas Research Network, 2012)  
 t(16;16)(q12;q13) FTO/HERPUD1 (Majewski et al., 2013)  
 t(16;16)(q23;q24) JPH3/OSGIN1 (Cancer Genome Atlas Research Network, 2012)

t(16;22)(p12;q11) POM121L4P/LCMT1 (Cancer Genome Atlas Research Network, 2012)  
 t(17;17)(p13;p11) PIGL/RABEP1 (Cancer Genome Atlas Research Network, 2012)  
 t(17;17)(p11;q11) AKAP10/PSMD11 (Cancer Genome Atlas Research Network, 2012)  
 t(17;17)(p11;q11) KIAA0100/ALKBH5 (Cancer Genome Atlas Research Network, 2012)  
 t(17;17)(q23;q23) RPS6KB1/VMP1 (Majewski et al., 2013)  
 t(18;22)(q12;q11) CDC45/RIT2 (Cancer Genome Atlas Research Network, 2012)  
 t(19;19)(p13;p12) UNC13A/ZNF492 (Cancer Genome Atlas Research Network, 2012)  
 t(19;19)(q13;q13) BCL3/HIPK4 (Cancer Genome Atlas Research Network, 2012)  
 t(19;19)(q13;q13) SIPA1L3/CD22 (Cancer Genome Atlas Research Network, 2012)  
 t(19;21)(p13;q22) ITSN1/ZNF490 (Cancer Genome Atlas Research Network, 2012)  
 t(19;22)(p12;q11) MMP11/ZNF714 (Cancer Genome Atlas Research Network, 2012)  
 t(20;20)(q11;q13) ADNP/DLGAP4 (Cancer Genome Atlas Research Network, 2012)  
 t(20;22)(q11;q12) PISD/RBL1 (Cancer Genome Atlas Research Network, 2012)  
 t(22;22)(q11;q11) THAP7/PRODH (Cancer Genome Atlas Research Network, 2012)  
 t(22;22)(q12;q12) APOL3/ISX (Cancer Genome Atlas Research Network, 2012)  
 t(22;22)(q12;q12) MCM5/TOM1 (Majewski et al., 2013)

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*This article should be referenced as such:*

Huret JL. Lung: Translocations in Squamous Cell Carcinoma. *Atlas Genet Cytogenet Oncol Haematol.* 2015; 19(8):545-549.

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