

**Lung cancer** is the leading cause of cancer-related death worldwide. The main lung cancer histological subtypes are small cell lung cancer (**SCLC**) and non-small cell lung cancer (**NSCLC**), being NSCLC the most common (80-85%). NSCLC is classified into adenocarcinoma (ADC), squamous cell carcinoma (SCC) and large-cell carcinoma (LCC). **ADC** histological subtype accounts for more than 50% of all lung cancers, **SCC** for approximately 30%, and **SCLC** for 10-15% of them. Cell and animal preclinical models are essential for evaluating the efficacy of specific drugs targeting driver mutations or immune-checkpoints. Both chemically induced mouse models (ChemMMs) of specific lung cancer subtypes and genetically engineered mouse models (GEMMs) may guide the so called precision medicine. We have specific models for **ADC**, **SCC** and **SCLC**, which is important because clinical therapies are frequently restricted to particular histological subtypes. In the case of **SCC**, there are no validated transgenic mouse models that uniquely reproduce SCC tumors. In fact, the N-nitroso-tris-chloroethylurea (NTCU) model is at present the only validated mouse model of lung SCC.

### List of lung cancer available cell lines

	NSCLC		SCLC
	ADC	SCC	
<b>ChemMMs (syngeneic)</b>	<b>UN-ADC12</b> (urethane) <b>Lacun 2 and 3</b> (NDMA + silica)	<b>UN-SCC679 and UN-SCC680</b> (NTCU)	
<b>GEMMs (syngeneic)</b>	Mouse <i>Kras</i> GEMMs <i>Kras</i> LA2 (LKR10, LKR13), <i>Kras</i> LSLG12D (LSZ1-5), <i>Kras</i> LSLG12D, p53f/f (389n1, 482n1) and <i>Kras</i> LSLG12D p53mut/+ (393P, 344SQ)		<b>KP1, KP3, KP11 and 5B</b>
<b>Human cell lines</b>	14 commercially available ADC cell lines	10 commercially available SCC cell lines	7 commercially available SCLC cell lines

#### ✓ ChemMMs

- **ADC:** Urethane injection. This model recapitulates in A/J strain mice the histopathological features of human lung ADC; glandular differentiation and immunohistochemical staining of TTF-1. A **syngeneic** cell line (UN-ADC12) harbouring a *Kras* mutation has been derived from this model.
- **ADC:** NDMA+silica. This model is developed by the combination of inflammation (induced by silica instillation) and tobacco-related lung carcinogenesis (N-Nitrosodimethylamine; NDMA) in BALB/c mice. Two **syngeneic** cell lines (Lacun2 and Lacun3) harbouring *Kras* mutations and *Wwox* deletion were derived.
- **SCC:** N-nitroso-tris-chloroethylurea (NTCU). Lung SCC tumors were induced by NTCU treatment (skin painting) to 8-week-old A/J mice twice a week for 20 weeks. The tumor **syngeneic** cell lines UN-SCC679 and UN-SCC680 were derived from these SCC tumors.

#### ✓ GEMMs

- **ADC:** Cell lines from *Kras* mutated mouse ADC tumors were established from different genetically-engineered mouse models (GEMMs) including *Kras*LA2, *Kras*LSLG12D, *Kras*LSLG12D; p53f/f and *Kras*LSLG12D; p53mut/+ mice.
- **SCLC:** Cell lines of SCLC mouse tumors were derived from *Rb*<sup>-/-</sup>; p53<sup>-/-</sup> mice.

#### ✓ Tumor models

- Subcutaneous xenograft models. i.e. Human cell lines into immune compromised mice
- Orthotopic lung ADC models: i.e. intratracheal or oropharyngeal instillation of lung cancer cells directed to the lungs
- Models of metastasis: metastasis models after heart, intratibial or vein injection
- Tumor cell detection by microCT, microPET, bioluminescence, X Ray etc.



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# Lung cancer Models Animal Models

## Recent Publications

1. Larrayoz et al. 2014 EMBO Molecular Medicine 6:539-550
2. Bleau et al. 2014 International Journal of Cancer 1;135:2516-27
3. Freire et al. 2013 Neoplasia 15: 913-924
4. Azpilikueta et al. 2016 JTO 11:524-536
5. Vallejo et al. 2017 Nature 8:14294
6. Ajona et al. 2017 Cancer Discov 7:694-703
7. Gettinger et al. 2017 Cancer Discovery 1:1420-1435
8. Ajona et al. Am J Respir Crit Care Med. 2018