- Lung cancer is the **leading cause of cancer death** worldwide.
- Prognostic markers may guide treatment decisions to improve survival of patients with lung cancer.
- **RNA metabolism score** is a five-gene expression signature for the prognostic evaluation of patients with early stage lung cancer.
- **Indication:** to determine the **risk of recurrence in surgically-treated lung cancer patients**.

Scope of the Problem

- Non-small cell lung cancer (NSCLC) accounts for 80-85% of all lung cancer cases and includes lung adenocarcinomas (ADC), the most frequent type of lung cancer.
- Surgery is the treatment of choice for early stage NSCLC. However, patients are at substantial risk for recurrence even after complete surgical resection (55%-70% of them will relapse within 5 years of diagnosis).
- To reduce the risk of recurrence, adjuvant chemotherapy is recommended for patients with resected stage II-IIIA lung cancer, although its benefit is low. The use of chemotherapy in stage I patients is still controversial.

Clinical Need

- The current staging system is not sufficient to determine the most appropriate treatment for each resectable lung cancer patient.
- A more accurate method for the **identification** of **early-stage patients** likely to have **more aggressive tumors** with occult metastases at the time of diagnosis is needed.
- Molecular prognostic markers may be used to identify those patients with surgically-treated NSCLC who are at high risk of developing regional or distant metastases and would benefit from adjuvant therapy.

Prognostic Marker Identification

- The RNA metabolism is involved in the pathogenesis of lung cancer.
- We have identified five RNA metabolism-related genes with prognostic value in patients with lung ADC.
- An **RNA metabolism score** based on the expression of these five genes has a strong prognostic capacity in these patients.

Prognostic Marker Validation

- The RNA metabolism score provides **independent prognostic information for recurrence free survival and overall survival in patients with lung ADC**.
- The score is able to differentiate high risk from low risk individuals in stages I and II, separately.
- The score is also able to differentiate risk populations of **women with breast cancer**.
- These results have been obtained using data from six independent patient's cohorts (a total of 534 lung cancer patients and 589 breast cancer patients).
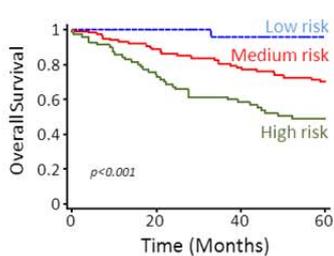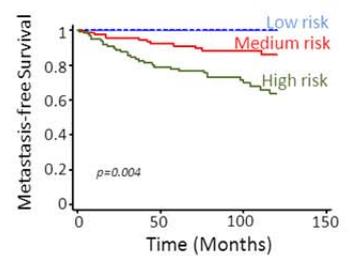

Survival curves of 213 patients with lung ADC divided by the RNA metabolism score
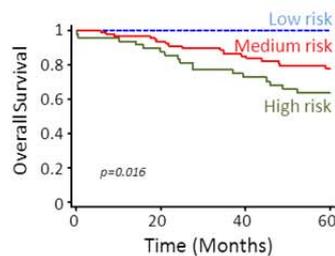
Survival curves of 157 patients with stage I lung ADC divided by the RNA metabolism score
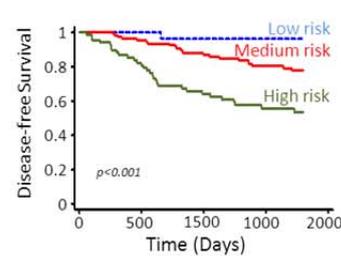
Recurrence curves of 204 patients with lung ADC divided by the RNA metabolism score

Metastasis curves of 200 patients with breast cancer divided by the RNA metabolism score

Competitive Advantage

- The prognostic information provided by the RNA metabolism score is independent of the tumor stage.
- The score retains its prognostic capacity in very early lung cancer stages (stage I).
- The score is based in only five genes, helping in its successful translation to the clinical practice.
- The RNA metabolism score can be applicable to other cancer types, such as breast cancer.

Intellectual Property	Methods and reagents for the prognosis of cancer. PCT/EP2013/062966. 21.06.2013 (licensed to Digna Biotech SL).
Reference	Identification of novel deregulated RNA metabolism-related genes in non-small cell lung cancer. *Plos One* 2012; 7: e42086.