Lung adenocarcinoma is the most sensitive cell line. Depletion of hSSB1 was associated with lung cancer cell death in vitro and in vivo.

hSSB1 depletion enhanced cell death in cisplatin sensitive and resistant cells. An isogenic H460 cell line pair: cisplatin-sensitive (H460 parental) and cisplatin-resistant (H460 resistant) was generated. hSSB1 inhibition using an in-house developed oligonucleotide, DKLS02, that interferes with hSSB1 DNA binding activity demonstrated significantly reduced cell proliferation in vitro (F) with a more profound effect in the cisplatin-resistant H460 cell line (purple lines).

Lung cancer is the leading cause of cancer death worldwide with an estimated 20% chance of survival 5 years after diagnosis. Non-Small Cell Lung Cancer (NSCLC) is the most common type of lung cancer (~80%) and can be divided in sub-groups: adenocarcinoma, squamous cell carcinoma and large cell non squamous carcinoma.

The hallmark of this malignant disease is its genomic instability leading to tissue invasion, metastasis, resistance to chemotherapy (notably cisplatin).

hSSB1 is a ‘guardian of the genome’ protein with a key role in the detection and repair of:
- Replication fork arrest
- Oxidative stress damage
- DNA double-strand breaks


**Aim**

The objective of our study is to assess the potential of hSSB1 as:
- a marker for lung cancer prognosis
- a target for new lung cancer therapy

**Background**

Lung cancer is the leading cause of cancer death worldwide with an estimated 20% chance of survival 5 years after diagnosis. Non-Small Cell Lung Cancer (NSCLC) is the most common type of lung cancer (~80%) and can be divided in sub-groups: adenocarcinoma, squamous cell carcinoma and large cell non squamous carcinoma.

The hallmark of this malignant disease is its genomic instability leading to tissue invasion, metastasis, resistance to chemotherapy (notably cisplatin).

hSSB1 is a ‘guardian of the genome’ protein with a key role in the detection and repair of:
- Replication fork arrest
- Oxidative stress damage
- DNA double-strand breaks


**Results**

**A** Lung cancer 
Lung adenocarcinoma

**B** Nuclear staining

**C** Time (months)

**D** Depletion of hSSB1 increases lung cancer cell death. hSSB1 was depleted by a specific siRNA in a panel of lung cancer cells (D). hSSB1 depletion led to decreased cell survival (E), measured by cell proliferation (full columns), with adenocarcinoma H1299 being the most sensitive cell line. Depletion of hSSB1 did not significantly increase cell sensitivity to a low dose of cisplatin (0.5 μM, dashed columns), except for H460 cells.

**E** Adenocarcinoma

**Material and methods**

We analysed hSSB1 mRNA expression from available online databases and hSSB1 protein expression in a TMA through immunohistochemistry staining using an in-house raised anti-hSSB1 antibody. We explored the impact of hSSB1 expression on NSCLC cell line sensitivity to cisplatin (measured by cell proliferation) on a panel of 3 adenocarcinoma (HCC827, H2228 and H1299), a squamous carcinoma (H226) and a large cell non squamous (H460) cell lines. We depleted hSSB1 with specific small interfering (si)RNA. An oligonucleotide, DKLS02, that interferes with hSSB1 DNA binding activity demonstrated significantly reduced cell proliferation in vitro (F) with a more profound effect in the cisplatin-resistant H460 cell line (purple lines).

**Conclusion**

Our results indicate that hSSB1 is a prognostic factor in NSCLC: high levels of mRNA and protein expression are associated with a worse outcome. Moreover, targeting hSSB1, as indicated by the siRNA experiments, may prove an effective strategy for the treatment of NSCLC and have a role in reversing platinum resistance.

Pre-clinical assessment of hSSB1 inhibition by our drug DKLS02 in vitro and in vivo showed a significant inhibition of NSCLC tumour growth, validating hSSB1 as a novel DNA damage response therapeutic target.