of secondary prevention on discharge were then sequentially added to models to assess the extent to which they explained the mortality difference.

Results 300,146 patients with a first MI were identified. 34,027 (11.3%) had COPD. In-hospital mortality was greater for COPD patients after a STEMI (see Table 1), this difference was reduced after adjusting for in-hospital factors. Mortality was also greater for COPD patients at 180 days; this was not reduced after adjustment for in-hospital factors, but was reduced after adjusting for use of secondary prevention. In-hospital mortality was also greater for COPD patients after a non-STEMI, this was reduced after adjusting for in-hospital factors. Mortality at 180-days after a non-STEMI was greater for COPD patients, this was reduced after adjusting for in-hospital factors, but not after adjusting for use of secondary prevention.

Conclusions Improved recognition and timely use of reperfusion treatments after a STEMI may significantly reduce the in-hospital mortality for COPD patients. Longer term mortality in COPD patients after a STEMI may be improved by increased use of secondary prevention drugs. Increased use of timely angiography may improve mortality for COPD patients after a non-STEMI.

REFERENCE

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Scientific advances in lung cancer

S108 MIF AS THE KEY REGULATOR FOR MESENCHYMAL STEM CELLS HOMING TO TUMOURS BY 3D AND *IN VIVO* LUNG METASTASIS MODELS

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Mesenchymal stromal cells (MSCs) are inherently tumour-homing and can be isolated, expanded and transduced, making them viable candidates for cell therapy. This tumour-tropism has been used to deliver anti-cancer therapies to various tumour models in several organs. In a previous study we have shown that MIF is the key director of MSC migration and infiltration towards tumour cells. We have shown this major role for MIF (mainly via CXCR4), using *in vitro* migration and invasion assays, in presence of different receptor inhibitors and achieving a drastic decrease in both processes using MIF inhibitor. Importantly we show that knock down of either CXCR4 or MIF abrogates MSC homing to tumours in an *in vivo* pulmonary metastasis model, confirming the *in vitro* 2D and 3D assays. In this study we define the mechanism behind MIF stimulation of MSC homing to tumours. We show that MIF upregulates other cytokines involved in chemotaxis, such as IL6, IL8 and CCL2 and upregulates MIF as well, amplifying the initial trigger and generating a positive feedback loop. However when inhibiting those cytokines individually, we never achieved a decrease in migration as drastic as for MIF inhibition. This suggests that the up-regulation of this set of cytokines would lead to chemoattraction of leucocytes to the site of the tumour, which was observed in a 3D model. Therefore, MIF trigger is amplified by its own upregulation in MSCs via a positive feedback loop, confirming again our previous findings and its key role as a regulator of MSC homing to tumours. This improved understanding of MSC tumour tropism will further enable development of novel cellular therapies for cancers.

S109 MESENCHYMAL STEM CELLS EXPRESSING FULL LENGTH TRAIL – A PROMISING THERAPY FOR CANCER

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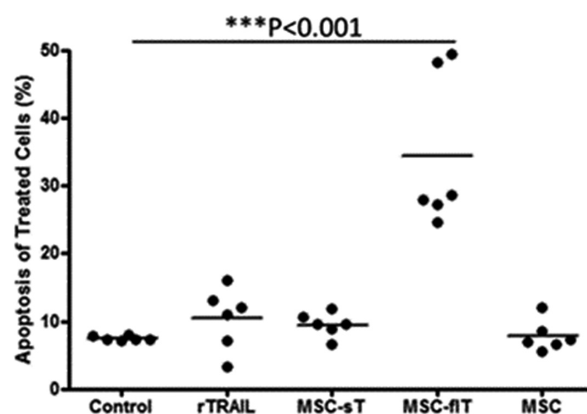
Bone marrow derived mesenchymal stem cells (MSC) are promising tools for lung cancer therapy considering their tendencies for tumour homing and low immunogenicity. Tumour necrosis factor related apoptosis inducing ligand (TRAIL) is a pro-apoptotic protein that induces selective apoptosis of tumour cells, while sparing normal cells. Therefore, it is expected that MSCs engineered to produce TRAIL will home to and kill cancer cells.

In this study, two lentiviral vectors were constructed to express the full-length (flT) or a truncated soluble form of TRAIL (sT) driven by a CMV promoter/enhancer. A secretion targeting sequence and an isoleucine zipper (ILZ) peptide were sequentially added to the N-terminal of the soluble TRAIL to produce secreted and trimerised TRAIL. TRAIL lentiviruses were prepared and human BM-MSCs were transduced with a multiplicity of infection (MOI) of 2. FACS analysis by anti-TRAIL antibody staining demonstrated that over 99% of flT or sT viruses transduced cells are positive for TRAIL expression. TRAIL expression was further confirmed by Western blotting and ELISA assays. The flT or sT expressing MSCs both showed similar level of cellular TRAIL expression (~350 ng TRAIL per 1 mg of total cellular protein).

Co-culture of cancer cells with transduced MSCs determined the cancer killing efficacy of MSCs expressing flT or sT. Twenty cancer cell lines were tested and classified into four TRAIL response groups; high, medium, low, and no sensitivity to recombinant TRAIL (rTRAIL) at the concentration of 50 ng/ml. At the co-culture ratio of 4:1 cancer to MSC cells, MSC-sT treatment showed no or only marginal cancer cell killing effect, in contrast, MSC-flT showed promising effects on all tested cell lines, with an apoptosis induction rate ranging between 35–75%. In groups designated as high, moderate and low, MSC-flT are as effective as rTRAIL and induced marked cell death ($p < 0.001$) in cell lines which showed no sensitivity to rTRAIL (Figure).

In conclusion, these results demonstrate MSC-flT is a promising cell therapy and have great potential for clinical treatment of lung cancers and pleural metastases.



Abstract S109 Figure 1 MSC-flT cells induce apoptosis in recombinant TRAIL-resistant cancer cells. Six rTRAIL-resistant cancer cell lines were treated with 50 ng/ml rTRAIL, MSC, MSC-sT and MSC-flT cells for 24 h. Apoptosis was quantified by Annexin V/DAPIFACS

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