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Transcriptomic profiling the microenvironment in primary melanomas

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The quantity of stroma is reported to be hazardous in many cancers (e.g. colon cancer)[1] whilst it is protective in others (e.g. oestrogen-receptor positive breast cancer).[2] We previously reported the protective effect of stromal content in 246 primary melanomas.[3] Here we report its transcriptomic correlates.

The percentage of stroma (POS) was recorded for 702 primary melanomas, using RandomSpot©[4] and ranged from 0 to 98%, median 33%. ESTIMATE was used to calculate tumour, immune and stromal cell scores.[5] Cox proportional hazards models were used to evaluate factors predictive of melanoma-specific death. Linear regression was used to assess the association between POS and the whole-genome transcriptome. Pathway enrichment analysis was performed using Metacore™.

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Age, sex, AJCC stage~~, tumour infiltrating lymphocytes (TILs)~~ and POS were significant prognostic factors in univariable analyses. Multivariable analysis of time to melanoma-specific death confirmed that POS was an independent prognostic factor, adjusting for age, sex and~~,~~ AJCC stage~~ and TILs~~ (HR 0.98 per percentage of stroma, p<0.0005~~=0.002~~ 95%CI 0.98~~7~~-0.99). POS was positively correlated with ESTIMATE's stromal score. Metacore™ analysis revealed upregulation of immune pathways in stromally rich tumours, including *LCK* and genes associated with MHC Class II and ICOS pathways and downregulation of cell cycle pathways.

We have shown that for every percentage increase in stroma there was a 2% decrease in melanoma-specific death. Transcriptomic profiling revealed that increasing stroma was associated with increased immune responses and reduced cell division.

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