Tumor growth characteristics of non-small cell lung cancer model LXFA 923 in humanized NSG mice

E. Oswald[1], , K. Klingner[1], D. Lenhard[1], G.Niedermann[2], J.B. Schüler [1]

[1] Department for Tumorbiology, Oncotest GmbH, Am Flughafen 12-14, 79108 Freiburg,
[2] Sektion Molekulare Radioonkologie, Klinik für Strahlenheilkunde, Universitätsklinikum Freiburg

Introduction

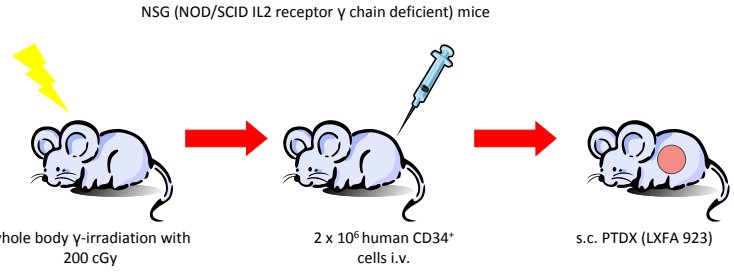
Patient-derived tumor xenografts (PDX) played a major role in the development of new cancer therapies and their strengths and weaknesses have gradually been elucidated.
One major drawback of PDX is the lack of an immunological competent host. To overcome this hurdle we "humanized" NSG mice and examined tumor growth characteristics of non-small cell lung cancer (NSCLC) PDX LXFA 923.
In parallel we monitored the presence of human and murine immune cells in different compartments of the mouse.

Materials and Methods

$2x10^6$ CD34+ cells were isolated from healthy donors and injected intravenously (i.v.) into sub-lethally irradiated NSG mice (n=8).
After 8 weeks LXFA 923 (NSCLC; p53 wt, kras mut, lkb mut) tumor material was transplanted subcutaneously into the humanized NSG mice.
Murine peripheral blood was examined by flow cytometry for common murine (mCD56, mCD14,mCD3) and human (hCD14, hCD3, hCD56, hCD19) markers expressed on immune cells once weekly.
At the end of the experiment tumors were analyzed for human cancer (CD44, CD133, CDCP1, CD166, CD24) and immune cell markers (hCD14, hCD3, hCD56, hCD19) by flow cytometry.
Parts of the tumors were fixed in Formalin paraffin embedded sections were cut and stained with Hematoxylin and Eosin (H&E).

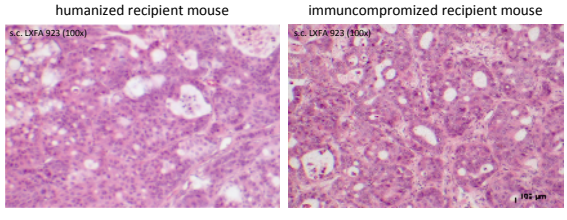
Results

Non-small lung cancer model LXFA 923 in humanized NSG mice



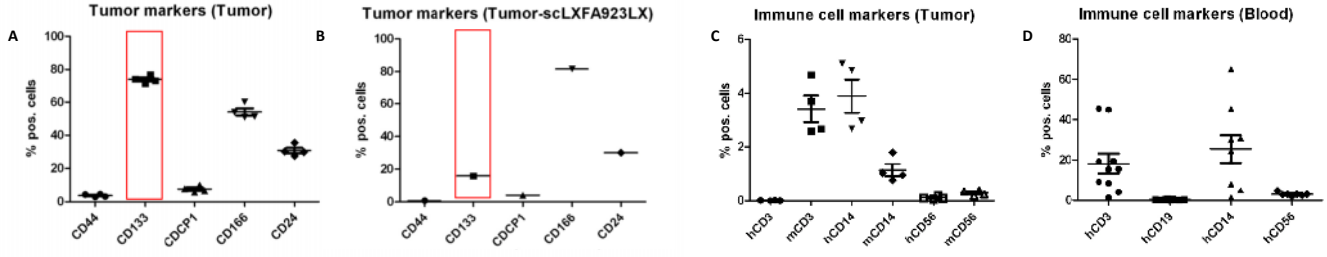
$2x10^6$ $CD34^+$ cells were isolated from healthy donors and injected intravenously (i.v.) into sub-lethally irradiated NSG mice (n=8). After 8 weeks LXFA 923 tumor material was transplanted subcutaneously (s.c.) into the humanized NSG mice.

No differences were determined between NSCLC LXFA 923 propagated in conventional or humanized mice concerning the histological architecture determined by H&E stain



Subcutaneous transplanted NSCLC LXFA 923 tumors of humanized NSG mice or control mice were embedded in paraffin and stained with Hematoxylin and Eosin (H&E).

Flow cytometry analysis of xenograft NSCLC (LXFA 923: p53 wt, kras mut, lkb mut) and peripheral blood of humanized NSG mice



A Cell suspensions of the solid LXFA 923 (n=4) tumor grown on humanized NSG mice were analysed for common tumor markers. **B** Cell suspensions of the solid LXFA 923 tumor (n=1) grown on control mice were analysed for common tumor markers. **C** Cell suspensions of the solid LXFA 923 tumor (n=4) were analysed for (mouse and human) T cell, monocyte and NK cell markers. **D** Peripheral blood of the humanized NSG mice (n=10) was analysed for (human) T cell, monocyte and NK cell markers.
All data were generated by Flow cytometry analysis; percentages of positive stained cells are shown.

Conclusions

- Generation of a humanized PDX model of NSCLC was successfully performed.
- The new model systems allows the investigation of interaction of tumor cells with human immune cells as well as the with murine stroma.
- CD133 could develop as a good marker for tumor consistency in LXFA 923 maybe as well in other NSCLC models.
- Humanized mice may be suitable for transplantation of addtl. PDX to reflect more closely the immunological status tumor of cancer patients.
- These models should facilitate the development of new drugs targeting/including the host immune response.

Acknowledgements

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