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Molecular Oncology

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EACR 2024 Congress Abstracts

Contents

PROFFERED PAPER PRESENTATIONS 2

Top Abstracts 2

Symposium: Modulating the Tumour Microenvironment . 3

Symposium: Drug Resistance 5

Symposium: Mechanism-based Clinical Trials 6

Symposium: Precision Cancer Medicine in the Post-genomic Era 7

Joint EACR-ICSA Symposium: Senescence, Dormancy, and Related Cell States 8

Symposium: Metabolism and Cancer 9

Symposium: Cell-based Therapies 10

Joint EACR-AACR Symposium: Spatial Analysis of Tumours/Spatial Transcriptomics 12

Symposium: Mechanical Forces of Cancer 13

Symposium: Mechanisms of Tumour Metastases 14

Symposium: Targeting Mitochondria in Cancer 15

Symposium: Liquid Biopsies 16

Symposium: Drugging Tumour Suppressor Genes 17

Joint EACR-ESR Symposium: Imaging the Tumour Microenvironment 18

Symposium: Making Cold Tumours Hot 19

Symposium: Drugging the RAS Pathway 20

Joint EACR-EMBO Symposium: Modelling Cancer 21

Symposium: Ageing, Gender, and Cancer 22

POSTER PRESENTATIONS (Tuesday/Wednesday) 24

Bioinformatics and Computational Biology 24

POSTER IN THE SPOTLIGHT 42

Biomarkers in Tissue and Blood 43

Cancer Cell Biology 78

Cancer Genomics 164

POSTER IN THE SPOTLIGHT 178

Carcinogenesis 192

Drug Resistance 199

POSTER IN THE SPOTLIGHT 224

POSTER IN THE SPOTLIGHT 231

POSTER IN THE SPOTLIGHT 231

Epigenetics 236

POSTER IN THE SPOTLIGHT 243

Experimental/Molecular Therapeutics, Pharmacogenomics 245

Immunotherapy 291

POSTER IN THE SPOTLIGHT 298

POSTER IN THE SPOTLIGHT 304

POSTER IN THE SPOTLIGHT 307

Molecular and Genetic Epidemiology 314

Prevention and Early Detection 318

Radiobiology/Radiation Oncology 330

Signalling Pathways 337

Translational Research 351

Tumour Biology 383

Tumour Evolution and Heterogeneity 439

Tumour Immunology 445

POSTER IN THE SPOTLIGHT 463

LATE-BREAKING ABSTRACTS 481

Proffered Papers

10-minute talks awarded for the highest scored abstracts, embedded in the scientific symposia sessions. These presentations are not accompanied by a poster.

Posters in the Spotlight

Tuesday 11 June, 18:15 - 18:40, Poster and Exhibition Hall
Wednesday 12 June, 18:15 - 18:40, Poster and Exhibition Hall

Dedicated sessions taking place in the spotlight area within the Poster and Exhibition Hall. Poster presenters with high scoring abstracts will give short presentations of up to 5 minutes each. Their posters will also be available to view during the Poster Discussion Sessions.

Late-breaking Abstracts

Late-breaking abstracts are those for which full data were not available at the time of the regular abstract deadline.

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CD45+cells and IFN-γ CD8+ producing cells in the anti-MIF + anti-PD-1 treated group compared to the other groups.

Conclusion

This information confirms that blocking MIF partially improves the outcome. However, these results could be further improved by modifying the delivery system and directing the therapy toward the tumors to increase its accumulation and prevent its sink in the periphery due to circulating MIF.

EACR2024-1147

Generation of a novel anti-EGFR monoclonal antibody CC4-B3-G3-H10 against Epidermal Growth Factor Receptor dimerization domain

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Introduction

EGFR is a transmembrane glycoprotein that constitutes one of four members of the ErbB family of tyrosine kinase receptors. Binding of EGFR to its ligands leads to autophosphorylation of the receptor tyrosine kinase and subsequent activation of signaling pathways involved in the regulation of physiological events such as cellular proliferation and differentiation. The sophisticated oncogene features of EGFR have made it an attractive target. Efforts to develop more effective therapeutic or diagnostic agents against EGFR are constantly ongoing. This study aimed to develop, characterize, and examine the effectiveness of a novel anti-EGFR monoclonal antibody against the EGFR dimerization region. Thus, even if the ligand binds there will be no dimerization and activation of EGFR and downstream pathways.

Material and Methods

Mice were immunized with a 20.24 kDa recombinant antigen of 824-1251 nucleotides encoding EGFR domain 2. Hybridomas were grown and selected by using a methylcellulose-based semi-solid selective medium system. During the selection process, anti-EGFRd2-producing mAb was demonstrated with a unique workflow by multistep immunoblotting and ELISA assays. The mAb was purified and then subjected to isotyping and affinity testing. Biological activity was monitored by real-time cell analyses to show the antibody's cellular inhibition efficacy on various cancer cells. Relative levels of 17 different phosphorylated amino acids were identified in EGFR and other ErbB family members with human EGFR phosphorylation antibody array.

Results and Discussions

Soluble recombinant EGFRd2 protein was produced with a high yield (0.5 mg/mL) and purity. 21 out of 209 hybridomas were detected specifically against EGFRd2. After further passages, four hybridomas were identified as stable and potent secretors. Then a stable clone was developed which produced the IgG1 kappa type anti-EGFR CC4-B3-G3-H10 mAb against EGFR dimerization site that binds its antigen with high affinity. It also has been shown to recognize endogenous EGFR. Cellular inhibition tests showed that it was at least as effective as Cetuximab. It was observed that EGFR (Tyr845), ErbB2 (Tyr1112), and ErbB2 (Ser1113) amino acids were endogenously phosphorylated in Caco-2 cells and Tyr845 and Tyr1112 were significantly decreased and there was no significant change at the Ser1113 level. Non-endogenous ErbB2 (Tyr877) increased significantly.

Conclusion

We conclude that novel CC4-B3-G3-H10 mAb has capacity for diagnostic applications and promising for therapeutic area.

EACR2024-1148

The endogenous T cell landscape is orchestrated by CAR-T cells and predictive of treatment response

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Introduction

T-cell redirecting immunotherapies, especially tumor-specific chimeric antigen receptor modified-T (CAR-T) cells, have transformed the treatment landscape for patients with hematological malignancies including multiple myeloma (MM). However, durable responses are observed in only a fraction of patients. To overcome treatment resistance and enhance the efficacy of CAR-T cells, a detailed understanding of their co-evolution with other components of the immune microenivronment is needed.

Material and Methods

We dissected the longitudinal CAR-T cell interactions that critically alter CAR-T cell function by investigating the immune microenvironment before, 1 month and 6 month after CAR-T cell treatment. We focused on anti-BCMA CAR-T cells in patients with MM as a model system, as the vast majority of this patient population experiences relapses. We used single cell transcriptome profiling to define the transcriptional states in CAR-T and endogenous T cells in combination with immune profiling and VDJ sequencing.

Results and Discussions

By dissecting the alterations in CAR-T cells and the CD8+ T cell compartment over time we observed persistent depletion of naïve-like CD8+ T cells, resulting in reduced differentiation potential and plasticity. We observed state-specific clonal expansion in the activated effector subset and identified pre-existing clones (39%), which we tracked over time and cell states. We defined novel transitional T cell states with an intermediate role in the T cell differentiation process. Transitional T cells T1 were associated with poor response, thus representing a potential target cell group to increase CAR-T cell efficacy. Additionally, we predicted TIM3/GAL9 as a highly specific interaction between endogenous T cells and CAR-T cells. TIM3 was highly specific to CAR-T cells by RNA and surface and its expression was correlated with worse clinical outcome. Our data indicate

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