

# NextCure NC410 is a Novel Immunomedicine for the Treatment of Solid Tumors

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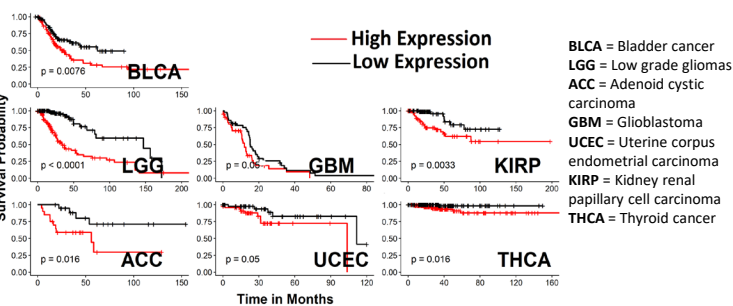
## Background

Abnormalities in the extracellular matrix of tumor microenvironments (TME) support tumor progression, lead to immune dysfunction, and provide targets for cancer therapeutics. Collagens are a primary component of the extracellular matrix. Abnormal levels of collagen in the TME have been proposed to disrupt anti-tumor immunity. LAIR-1 is an adhesion molecule and inhibitory receptor expressed on the cell surface of several immune cell subsets. LAIR-1 binding to collagens inhibits immune cell function. LAIR-2 is a soluble homolog of LAIR-1 that binds to and outcompetes LAIR-1 binding to collagens and serves as a natural decoy to promote immune function.

## Methods

Taking advantage of a natural decoy system, we designed a protein biologic, NC410, composed of LAIR-2 fused with the human IgG<sub>1</sub> Fc domain to target collagen-rich, immune excluded tumors and promote immune activation, infiltration and effector function.

## Overexpression of total collagens is associated with poor overall survival in several cancer types



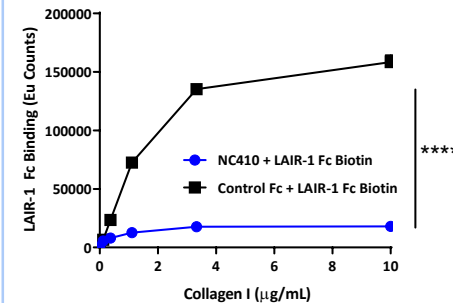
TCGA collagen expression for all 43 collagen chains were assessed together (total collagen) for contribution to overall survival (25% high and low quantiles). The estimate of overall survival was determined by Kaplan-Meier method. Cancer types with significant reduction in OS with high total collagen levels are shown.

## NC410 is a dimeric fusion protein of LAIR-2 and hlgG<sub>1</sub>, and blocks LAIR-1 binding to collagen

### NC410 Structure



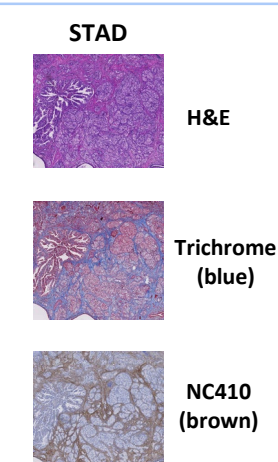
### Blocking LAIR-1 Binding



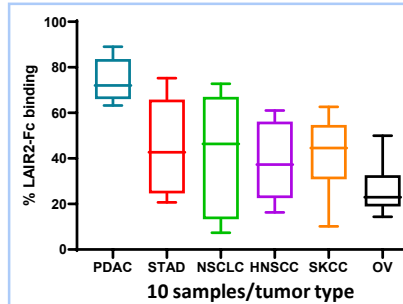
1 µg/mL LAIR-1 Fc Biotin + 10 µg/ml protein

## NC410 binds collagens most highly in immune excluded cancers

### Exemplary Staining

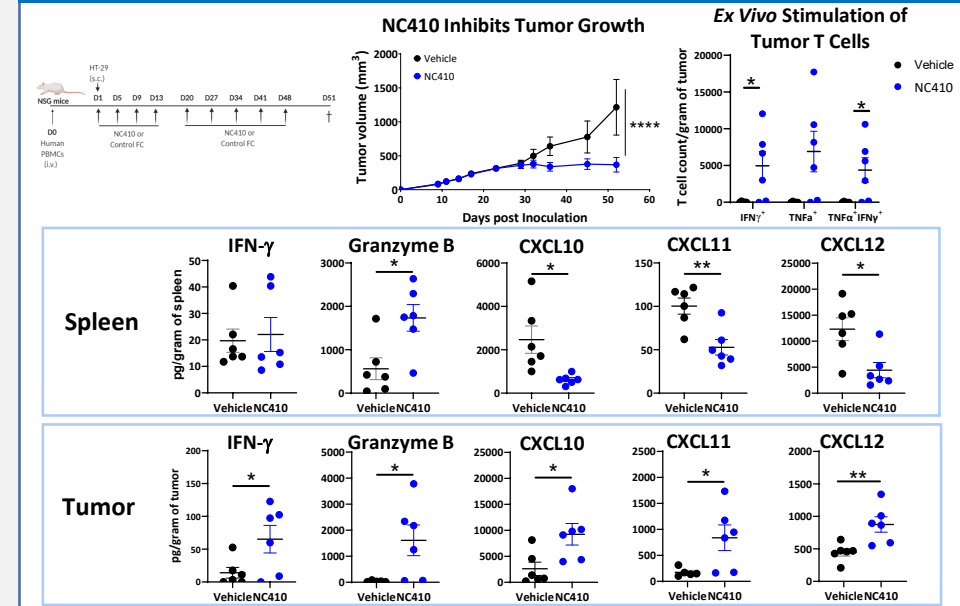


### Quantification of LAIR-2-Fc Staining

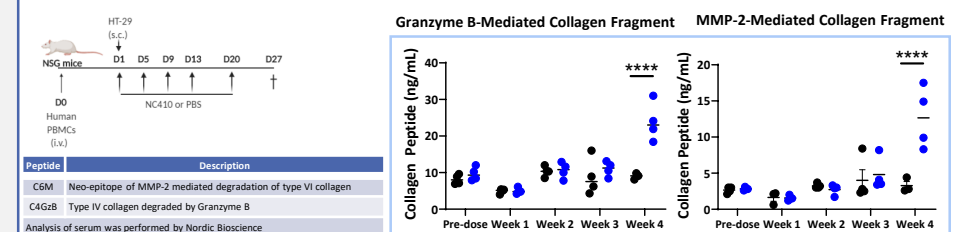


**HNSCC** = Head & Neck Squamous Cell Carcinoma  
**SKCC** = Squamous Cell Carcinoma  
**NSCLC** = Non-Small Cell Lung Carcinoma  
**OV** = Ovarian Serous Carcinoma  
**PDAC** = Pancreatic Ductal Adenocarcinoma  
**STAD** = Stomach Adenocarcinoma

## NC410 demonstrates anti-tumor activity and potentiates local and systemic anti-tumor T cell immunity



## Collagen degradative products indicative of immune activation and ECM remodeling are increased with NC410 treatment



## Conclusion

These data support NC410 as a novel therapeutic for targeting collagen-rich tumors and enabling normalization of the tumor-immune microenvironment. A FIH study (NCT04408599) has recently been initiated with NC410.