the samples is on-going with single-cell sequencing and digital spatial profiling.

Conclusions We believe this is the first report of immune profiling of in situ tumour microenvironment in a cancer patient with COVID-19. Our findings showed the presence of viral proteins in several tissues despite negative swab test result, and the ability to elicit ex vivo SARS-CoV-2-specific T cell responses through peptide stimulation experiments.

Ethics Approval This study was approved by Centralised Institutional Review Board of SingHealth; approval number 2019/2653.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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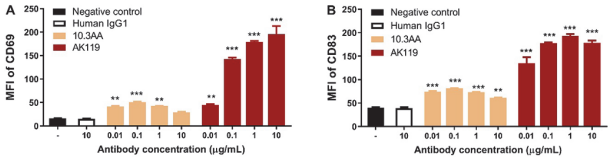
http://dx.doi.org/10.1136/jitc-2020-SITC2020.0475

476 AK119, A HUMANIZED ANTI-CD73 MONOCLONAL ANTIBODY, AS IMMUNOTHERAPY FOR COVID-19

[1]Tingting Zhong, [1]Zhaoliang Huang, [1]Xinghua Pang, [1]Na Chen*, [1]Konyew Kwek, [2]Chris Wynne, [1]Adam Konpa, [1]Xiaoping Jin, [1]Yu Xia, [1]Maxwell Zhongmin Wang, [1]Baiyong Li, [1]Yu Xia. [1]*Akeso Biopharma Co., Ltd., Zhongshan city, China*; [2]*Christchurch Clinical Studies Trust Ltd., Christchurch, New Zealand*

Background CD73, an ecto-5'-nucleotidase involved in ATP metabolism, converts AMP into adenosine. ATP could induce production of interferon-beta[1], which induces cellular resistance to viral infection and triggers apoptosis of virus-infected cells.[2] In COVID-19, SARS-CoV-2 causes severe respiratory syndrome by effectively inhibiting interferon activity,[3 4] leading to impaired anti-viral response. Moreover, lung injury seen in severe COVID-19 patients might be caused by excess adenosine.[5] Inhibition of CD73 is believed to increase extracellular ATP, thereby countering COVID-19. Furthermore, independent of its inhibitory effects on CD73, preclinical results from other anti-CD73 mAb suggested CD73 blockade activates lymphocytes, induced antibody production from B cells and enhanced lymphocyte trafficking,[6] thereby, stimulated the production of anti-SARS-CoV-2 antibodies leading to the rapid clearance of the virus.[7] We developed AK119, a humanized monoclonal antibody targeting CD73, as an immunotherapy agent for the treatment of COVID-19.



Abstract 476 Figure 1 AK119 induces up-regulation of CD69 and CD83 expression on B cells. PBMCs were incubated overnight with AK119 or 10.3AA. Flow cytometry analysis was performed with gating on B cells (CD19+CD3-) and mean fluorescence intensity (MFI) is reported for antibody staining of (A) CD69 or (B) CD83. One-way ANOVA, **P<0.01, ***P<0.001, vs Human IgG1 group.

Methods Evaluation of AK119 activity to bind to the CD73 antigen was performed by using ELISA, Fortebio, and FACS assay. The activity of AK119 to inhibit enzymatic activity of CD73 was evaluated by cell-based enzyme assay; and the activity of AK119 to induce internalization of CD73 and enhance CD69 and CD83 expression on B cell were performed by using FACS assays. We also investigated the potential of AK119 to promote immunoglobulin production from human B cells.

Results AK119 could effectively bind to human CD73 with high affinity, which is comparable or superior to 10.3AA, a leading anti-CD73 antibody, in protein-based assays. AK119 inhibited CD73 enzymatic activity on MDA-MB-231 cells (IC50_AK119, 27.60 nM; IC50_10.3AA, 15.99 nM) and U87-MG cells (IC50_AK119, 0.2448 nM; IC50_10.3AA, 0.0691 nM), with a higher maximal inhibition rates of 108.26% in MDA-MB-231 cells and 96.24% in U87-MG cells compared with 10.3AA (77.02% and 75.77%, respectively). AK119 effectively induced CD73 internalization in MDA-MB-231 cells and U87-MG cells, and the internalization rate of CD73 was 60.75% and 82.39%, respectively; for 10.3AA, the internalization rate was 50.53% and 73.65%, respectively. Moreover, AK119 could stimulate approximately 4–5 fold up-regulation of CD69 (figure 1A) and CD83 (figure 1B) that are markers of B cell activation; and, AK119 significantly promoted IgG production from B cells.

Conclusions In summary, in comparison to a leading CD73 antibody currently in clinical trial, AK119 demonstrated more complete CD73 inhibition; and more dramatic B cell activation and antibody production. Thus, A119 presented desirable preclinical bioactivities. The safety and pharmacokinetics of single ascending doses of AK119 will be evaluated in healthy volunteers in an upcoming Phase 1, First-in-Human study (NCT04516564).

Trial Registration NCT04516564

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http://dx.doi.org/10.1136/jitc-2020-SITC2020.0476

477 DEEP LEARNING TO DRIVE COVID-19 RAPID DRUG REPURPOSING

Sarah Kolitz *, Jason Kim, Jenny Zhang, Yoonjeong Cha, Sailaja Battula, Rebecca Kusko, Rajaraman Krishnan, Benjamin Zeskind, Howard Kaufman. *Immuneering Corp., Cambridge, MA, USA*

Background COVID-19 is a global public health crisis with no effective therapeutic strategies or vaccines available. The disease is caused by the SARS-CoV-2 virus, a novel coronavirus that enters cells through the ACE2 receptor. To rapidly identify existing drugs that might preferentially bind to the ACE2 receptor we sought to use an artificial intelligence platform to evaluate ~3,000 known drugs in the FDA approved drug library (Selleckchem).

Methods Fluency is a quantitative structure–activity relationship (QSAR) deep learning-based platform that evaluates small molecule drug binding to protein targets. All drug structures from the FDA approved library were evaluated for binding to the ACE2 receptor and re-filtered for preferential ACE2 vs. ACE1 receptor binding. Top hits were evaluated for specificity by predicting binding across the human proteome and filtered by evaluating rankings from each of two models along with average ranks and combined scores from both models. The drugs were then evaluated for classification, potential availability and prioritized for in vitro validation. Selected compounds were screened using a high-throughput SARS-CoV-2 cell-based assay as described previously (Jonsson *et al*. J Biomol Screen 2007 12: 33. DOI: 10.1177/1087057106296688). Plates are quality-controlled in each run using Z score and CV statistics. Positive controls consisting of cells only and negative controls consisting of virus were used to normalize the data. Individual drugs are added to each plate at a single dose with at least four doses tested. For titer reduction assays, VeroE6 cells are infected with virus at MOI of 0.1 for one hour to promote adsorption. After two days, the supernatant is harvested and the amount of virus in each well is measured using TCID50 or plaque assay.

Results We identified 25 top drugs that were predicted to bind to ACE2 receptors and could theoretically block SARS-CoV-2 cell entry. Of these drugs, we prioritized 12 drugs for validation covering multiple pharmacologic classes and after assessing drug availability (table 1). They included an ALK/EGFR inhibitor, JAK inhibitor, two electrolyte channel inhibitors, \an antibiotic, and several anti-viral drugs, ACE inhibitors and anticoagulants. Validation studies are in progress and viral inhibition and titer reduction data will be presented.

Conclusions Our data show that machine learning platforms can be used to rapidly identify existing drugs that may have activity against SARS-CoV-2 infection. This hybrid computational and experimental approach enables rapid discovery of drugs for clinical testing against COVID-19 and other emerging human diseases.

Acknowledgements We would like to thank Dr. Colleen Jonsson and Dr. Jeremy Smith at Oak Ridge National Laboratories and the University of Tennessee Regional Biocontainment Laboratory for assistance with in vitro validation studies.

Trial Registration N/A

Ethics Approval N/A

Consent N.A

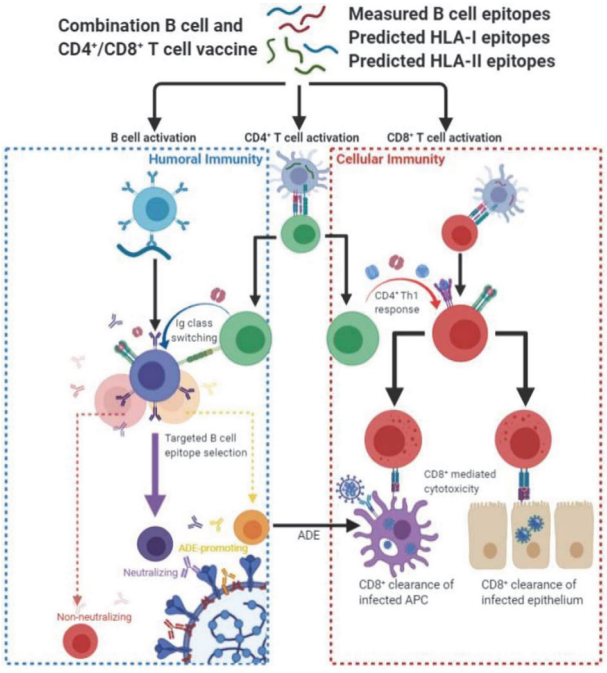
http://dx.doi.org/10.1136/jitc-2020-SITC2020.0477

478 TRANSLATION OF A THERAPEUTIC NEOANTIGEN VACCINE WORKFLOW TO SARS-COV-2 VACCINE DEVELOPMENT

[1]Christof Smith*, [1]Sarah Entwistle, [1]Caryn Willis, [1]Steven Vensko, [1]Wolfgang Beck, [1]Jason Garness, [1]Maria Sambade, [1]Eric Routh, [1]Kelly Olsen, [1]Brandon Carpenter, [1]Kaylee Gentry, [1]Maria Fadri, [1]Misha Fini, [1]Amber Washington, [2]Julia Kodysh, [2]Timothy O'Donnell, [3]Carsten Haber, [3]Kirsten Heiss, [3]Volker Stadler, [4]Erik Garrison, [5]Oliver Grant, [5]Robert Woods, [1]Mark Heise, [1]Benjamin Vincent, [1]Alexander Rubinsteyn. [1]*UNC Chapel Hill, Chapel Hill, NC, USA*; [2]*Icahn School of Medicine at Mount Sinai, New York, NY, USA*; [3]*PEPperPRINT GmbH, Heidelberg, Germany*; [4]*University of California, Santa Cruz, Santa Cruz, CA, USA*; [5]*University of Georgia, Athens, GA, USA*

Background There is an urgent need for a vaccine with efficacy against SARS-CoV-2. We hypothesize that peptide vaccines containing epitope regions optimized for concurrent B cell, CD4+ T cell, and CD8+ T cell stimulation would drive both humoral and cellular immunity with high specificity, potentially avoiding undesired effects such as antibody-dependent enhancement (ADE) (figure 1). Leveraging methods initially developed for prediction of tumor-specific antigen targets, we combine computational prediction of T cell epitopes, recently published B cell epitope mapping studies, and epitope accessibility to select candidate peptide vaccines for SARS-CoV-2 (figure 2).

Methods SARS-CoV-2 HLA-I and HLA-II ligands were predicted using multiple MHC binding prediction software. T cell vaccine candidates were further refined by predicted immunogenicity, viral source protein abundance, sequence



Abstract 478 Figure 1 Summary of combination CD4+/CD8+ T cell and B cell SARS-CoV-2 peptide vaccine. Humoral immunity (blue dashed box) is targeted through B cell and HLA-II epitopes, aimed at viral neutralization while avoiding non-neutralizing and ADE promoting targets. Cellular immunity (red dashed box) is targeted through HLA-I and HLA-II epitopes, aimed to clear virally infected cells

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