scRNA-seq on these samples. Following unbiased clustering, we observed and characterized five distinct fetal NK cell subsets in the umbilical cord blood and four fetal NK cell subsets in the corresponding umbilical cord tissue. Our findings revealed that HCMV+ fetal NK cells primarily consisted of mature NK cell subsets, while HCMV- fetal NK cells constituted the majority of the immature subsets. Importantly, we identified a unique subset of NKG2CHi fetal NK cells that were significantly elevated in the HCMV+ fetuses. Finally, we defined a group of transcription factors involved in the formation of antiviral fetal NK. DISCUSSION/SIGNIFICANCE: Here, we demonstrate that HCMV infection can induce the formation of distinct NK cell subsets and drive their unique transcriptional profiles. These findings have the potential to guide the development of an innovative NK cell immunotherapy that could help prevent fetuses from developing symptomatic cCMV.

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## BiP knockdown decreases antibody production in malignant and non-malignant plasma cells

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OBJECTIVES/GOALS: Numerous diseases, including AL amyloidosis, are due to expression of aberrant antibodies. Significant effort has gone into plasma cell toxic therapies with varying degrees of success, but no therapies preventing antibody synthesis have been developed. The goal of this study is to assess BiP targeting to prevent antibody secretion in plasma cells. METHODS/STUDY POPULATION: Using 4 multiple myeloma cell lines (KMS11, RPMI8226, ANBL-6, U266), we knocked down BiP expression with RnaseH dependent siRNA or subA toxin, a bacterial toxin that specifically cleaves BiP, and measured changes in unfolded protein and intracellular light chains by flow cytometry during drug induced ER stress created by the intracellular calcium depleting agent thapsigargin. BiP is the master regulator of the unfolded protein response (UPR), an ER stress pathway important for protein folding. BiP is also an ER resident protein folding chaperone important for proper antibody folding. We hypothesized that BiP downregulation will lead to decreased folded antibody in the cell, increased unfolded antibody and constitutive activation of the UPR. RESULTS/ANTICIPATED RESULTS: 1 to 4 hours after treatment with thapsigargin plus siRNA against BiP, levels of BiP are significantly decreased. The levels of intracellular light chains decrease, and the level of unfolded protein within the cells increases dramatically. Interestingly, in alignment with the UPR literature, 24 hours post treatment, these levels have normalized again in surviving cells. SubA treatment increased BiP expression by 4 hours, contrary to our hypothesis, and minimally increased unfolded proteins and minimally decreased intracellular light chains. We expect that further functional testing of antibody secretion by ELIspot assays will show decreased secretion of antibody with BiP siRNA treatment. Combination therapies with other UPR stressing agents may act synergistically to affect antibody production. DISCUSSION/SIGNIFICANCE: BiP knockdown reduces antibodies and boosts unfolded proteins. SubA toxin ineffectiveness likely stems from increased BiP due to feedback loops. Combining anti-BiP treatments with UPR stressing drugs like bortezomib may halt antibody synthesis and induce cell death. These findings support BiP as a viable drug target for antibody-related diseases.

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## Unitary neural correlates of self-control in pediatric transdiagnostic psychopathology*†

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OBJECTIVES/GOALS: Childhood psychopathology is a worsening public health crisis leading to negative life outcomes, including self-harm and suicide. Difficulty in self-control as early as 3 years old predicts psychopathology, but the mediating mechanisms of brain function are unknown. Here, we tested one mechanism: functional connectivity (FC) integration. METHODS/STUDY POPULATION: We studied a sample of 204 children [53 F/149 M/2 NC; mean age (SD)=11 years (1.7)] with diverse self-control difficulties (e.g., attention deficit disorder [n=80]; autism spectrum disorders [n=91]). We extracted a general factor of psychopathology ("p-factor") from the parent-reported Child Behavior Checklist. For participants with high quality fMRI data on 3 self-control tasks (n=79), testing flexibility, working memory, and inhibition, we calculated FC connectomes reflecting a general self-control state, and applied connectome predictive modeling (CPM) to reveal connections predicting overall task impairment. We then measured individual variance in cross-network integration of regions with the most predictive connections and tested for association with p-factor in a multiple linear regression. RESULTS/ANTICIPATED RESULTS: We repeated CPM 1,000 times with 10-fold cross validation to generate a distribution of accuracies for predicted vs. observed task impairment scores (mean r=0.25, permutation p=0.02). Connections selected a maximum of 10,000 times (10 folds * 1,000 repetitions) were strongly predictive of task impairment (r=-0.5, p<0.001), highlighting connectivity of canonical executive networks as well as the default mode network. Regions (n=22) with the top 5% most selected connections were in lateral parietal and frontal cortices and implicated motor control. Between-network integration, operationalized with the graph theory metric participation coefficient, of one of these regions in left posterior superior frontal gyrus significantly predicted p-factor ($R2=0.26$, $F(22,56) = 0.87$; $B = -0.49$, $p<0.05$). DISCUSSION/SIGNIFICANCE: A portion of dorsolateral prefrontal cortex, associated with executive control, explained individual variance in p-factor. We plan to test alternative predictive models. Identification of such a neuro behavioral mechanism underlying psychopathology may lead to novel intervention targets.

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## Beyond Antibiotics: Monensin and its Derivatives as Promising Anti-Breast Cancer Agents

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OBJECTIVES/GOALS: Although the approval of immune checkpoint inhibitors (ICIs) revolutionized the treatment of metastatic


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