Over the past decade, federal and private funders have made major investments in the evaluation of programs targeting language, pre-literacy and mathematics skills among young children at risk of school failure. In contrast, a new generation of interventions highlights the promise of targeting self-regulatory processes (such as executive function and attentional control) as a way to support early learning. This focus has been paralleled by recent advances in neuroscience linking poverty and the structure and function of cortical and striatal networks involved in self-regulation. The rationale and evidence for targeting self-regulation through early intervention will be presented in the Keynote Address. New directions in study design and program evaluation, drawing from recent innovations in prevention science, developmental science, and education science, will also be discussed.