**In vivo and in vitro characterization of discretion mutations**

During the past year, we made significant progress in the characterization of the dyskerin enzyme on three levels. First, using an allelic series that we created for this project, we demonstrated *in vivo* that the enzyme is indispensible for development, and it is necessary for protein synthesis, through its role in ribosome biogenesis. Second, using known mutations in dyskerin, we were able to demonstrate that certain mutations do not disrupt the composition of the complex per se, but they impair the active center, by indirectly inducing structural changes in the complex. Finally we performed mixed quantum mechanical/molecular mechanical calculations on the putative reaction mechanisms put forward in the literature and we propose a novel mechanism to explain the isomerization reaction catalyzed by the dyskerin molecule.