

TABLE OF CONTENTS

ABBREVIATION LIST	1
ABSTRACT	3
INTRODUCTION	5
CHAPTER 1	
The Nuclear Pore Complex: Structure and Function	5
Biology of a Complex Machine	5
Structure	5
Function	10
1. NPCs in nucleocytoplasmic transport: busy roads	11
2. NPCs as hubs for gene regulation	12
CHAPTER 2	
Nucleocytoplasmic Transport	17
Cellular Requirements and Therapeutic Implications in Cancer ...	17
Karyopherins and the Small GTPase Ran	18
Disruption of Protein Nuclear Export in Cancer.....	21
Selective CRM1 inhibitors	23
Targeted Inhibition of CRM1 in Leukemia Therapy	26
CHAPTER 3	
Leukemia	27
From Hematopoiesis to Leukemia	27
Leukemia: One Name, Several Diseases.....	30
Acute Myeloid Leukemia (AML)	31
Acute Lymphoblastic Leukemia (ALL)	35
AML and ALL: converging to the upregulation of HOX genes	38
NUP98 and NUP214 fusion transcripts in AML and ALL with poor prognosis	43
Publication 1	
On the Effects of Leukemogenic Nucleoporin Fusion Proteins in Nucleocytoplasmic Transport and Gene Expression.....	45
Publication 2	
NUP214 in Leukemia: It's More than Transport	72
GOALS OF THE RESEARCH PROJECT	93

RESULTS	95
Publication 3	
The Oncogenic Fusion Proteins SET-Nup214 and Sequestosome-1 (SQSTM1)-Nup214) Form Dynamic Nuclear Bodies and Differentially Affect Nuclear Protein and Poly(A) ⁺ RNA Export	97
Publication 4	
Targeted CRM1-Inhibition Perturbs Leukemogenic NUP214 Fusion Proteins and Exerts Anti-Cancer Effects in Leukemia Cell Lines with NUP214 rearrangements	115
Publication 5	
Disclosing the Interactome of Leukemogenic NUP98-HOXA9 and SET-NUP214 Fusion Proteins by a Proteomic Approach	156
GENERAL DISCUSSION & FUTURE DIRECTIONS.....	195
CONCLUSION OF THE RESEARCH PROJECT	206
In the Future	210
REFERENCES	212