1. Table of contents

2. Abstract 7

3. Introduction 8

3.1 Gene expression in eukaryotes
3.2 mRNA processing
3.2.1 Sequential splicing reactions
3.2.2 Alternative splicing
3.2.3 Alternative cleavage and polyadenylation
3.3 mRNA export pathways
3.3.1 NXF1/Tap-mediated export
3.3.2 Crm1-mediated mRNA export
3.4 mRNA quality control (QC)
3.5 Retroviral strategies to bypass mRNA QCs
3.5.1 The RRE-mediated mRNA export
3.5.2 The CTE-mediated export
3.6 The nuclear pore complex
3.7.1 The nuclear basket protein, Tpr
3.7.2 Functional aspects of Tpr
3.8 The aim of this study

4. Results..... 30

4.1. Detection of bulk mRNAs upon RNAi of Tpr
4.2. The establishment of a novel reporter system to analyze mRNA export
4.3. The detection of potential un-spliced mRNA leakages in the absence of Tpr using the triple reporter cell lines
4.4. The enrichment of a specific intermediate at the distinct splicing stages does not cause an increase in intron-based reporter activity in the absence of Tpr in interphase cells
4.5. Studying un-spliced mRNA leakage in the absence of Tpr using an exon-based leakage reporter cell system
4.6. The expression levels of intron-containing HIV-*gag* mRNAs are elevated by the depletion of Tpr in the presence of the CTE
4.7. Tpr amount required for the HIV-*gag* mRNA retention
4.8. The effect of exogenously expressed Tpr polypeptides on the HIV-Gag protein levels
4.9. The potential roles of the essential sites required for splicing in the Tpr-dependent HIV-*gag* mRNA regulation
4.10. The potential role of the HIV-*gag* ORF sequence in the Tpr-dependent HIV-*gag* mRNA regulation
4.11. The CTE-containing *Photinus luciferase* mRNAs are not monitored by Tpr
4.12. Further mapping of the HIV-*gag* segment involved in the Tpr-dependent nuclear retention of the HIV-*gag* mRNA
4.13. Investigation on whether Tpr might play a role in the subcellular distribution of other CTE-harboring transcripts, or of some distinct, alternatively spliced, intron-containing endogenous transcripts
4.14. Possible explanations for the Tpr-dependent regulation of un-spliced mRNAs

Dieses Werk ist copyrightgeschützt und darf in keiner Form vervielfältigt werden noch an Dritte weitergegeben werden.
Es gilt nur für den persönlichen Gebrauch.

4.14.1. Investigating the potential roles of the HIV inhibitory sequence (INS)-related proteins in the Tpr-dependent HIV-*gag* mRNA retention
4.14.2. Investigating a potential contribution of the NPC-binding proteins to the Tpr-dependent HIV-*gag* mRNA regulation
4.14.3 RNAi screening: the proteins potentially involved in the HIV-*gag* mRNA regulation
4.14.4 Searching for possible contributions of the positive candidates in HIV-*gag* mRNA regulation
4.14.5 Investigating a possible contribution of Tpr in the long non-coding RNA degradation pathway
4.14.6 Further attempts to gain insight into the Tpr-dependent mechanism of retaining CTE-containing HIV-*gag* transcripts in the nucleus
4.15. Proteins potentially involved in the Tpr-dependent mRNA export

5. Discussion..... 91

5.1. The establishment of stable reporter cell lines to monitor mRNA retention and export
5.2. Considering the possibility of un-spliced mRNAs occurring in mitotic cytosols due to mitotic NE disassembly and the effects on the analysis of mRNA export
5.3. A potential contribution of Tpr to bulk mRNA export
5.4. Tpr is involved in the regulation of the CTE-containing un-spliced mRNA export
5.5 In the Tpr-deficient cell, export of the HIV-*ga*g-CTE mRNAs appears to prevent them from being more quantitatively spliced or degraded
5.6. Which Tpr pool is responsible for preventing the HIV-*gag*-CTE mRNA export?
5.7. How many Tpr molecules are required for the prevention of HIV-*gag*-CTE mRNA export?
5.8. How does Tpr prevent the HIV-*gag*-CTE mRNA export?
5.9. Which Tpr domain is responsible for the suppression?
5.10. The difference of reporter systems between yeast and vertebrates
5.11 Perspective

6. Materials and Methods..... 108

7. Acknowledgement..... 123

8. Appendix..... 126

Appendix 1: HIV-gag sequences

Appendix 2: Supplement figures

Appendix 3: Table 4-2, and Table 4-3

9. References..... 135

Dieses Werk ist copyrightgeschützt und darf in keiner Form vervielfältigt werden noch an Dritte weitergegeben werden.
Es gilt nur für den persönlichen Gebrauch.