Introduction

Cisplatin is one of the most common anticancer drugs that are used to treat patient against various cancers. Cisplatin is the first platinum-based drug that was approved by FDA in 1978. Cisplatin has shown anticancer activity in a variety of tumors including ovarian, testicular, colorectal, lung, and head and neck cancers (Galluzzi et al., 2012). Cisplatin often results in successful treatment with partial responses or disease stabilization, however some patients are resistant to cisplatin-based treatment. High incidence of chemo-resistance has become the main limitation of cisplatin as anticancer drug.

In the early 1980s, new generation of platinum-based anticancer drugs were developed with the specific aim of reducing the side effects of cisplatin while still retaining its anticancer properties. There are some drugs that were successfully developed, but most of these drugs forms the same type of DNA adducts as cisplatin. For instance, carboplatin is one of the new generation of platinum-based anticancer drugs was approved by FDA in 1989 to treat ovarian cancer. However, most cisplatin-resistant tumors also fail to respond carboplatin because it has more or less the same mechanism of action as cisplatin. Researchers have been studying about anticancer drug resistance, as it is a big problem in treating tumors for cancer patients.

New anticancer drug that can kill cisplatin-sensitive and cisplatin-resistance cancer cells will be needed in the future. Thus *in vitro* assay that can serve the purpose of this experiment is very important, and to make this *in vitro* assay possible, the availability of cisplatin-sensitive and cisplatin-resistant cancer cell lines are crucial.

The objective of this thesis is to generate cisplatin-resistant HeLa cells that later can be used for screening for cytotoxic drugs, screening for drugs that may reverse the cisplatin-resistance to become cisplatin-sensitive cell lines, and also basic research such as investigating the mechanism and pathways involved in resistance and its reversal.