I. Introduction

Penicillium marneffei was first isolated from bamboo rats *(Rhizomys sinensis)* by Capponi in 1956 (Capponi *et.al.,* 1956). The fungus was identified by Segretain as a new species, *Penicillium marneffei,* in honor of Hubert Marneffe, director of the Pasteur Institute of Indochina (Segretain, 1959). *Penicillium marneffei* has been recognized since 1973 as an agent of natural infections among immunocompromised patients travelling in South-east Asia (Disalvo *et.al.*, 1973). Epidemics of penicilliosis marneffei have been reported since 1984 in southern China and Thailand among native healthy or immunocompromised patients as a systemic mycosis involving the entire reticuloendothelial system, and mimicking histoplasmosis (Drouhet, 1993). The most common presenting symptoms of penicilliosis marneffei were fever, anemia, weightloss and skin lesions (Supparatpinyo *et.al.*, 1994). This mycosis is a treatable disease but delay of treatment may be fatal. Without treatment, the rate of mortality was 91.3% in non-AIDs patients and 100% in AIDs patients (Drouhet, 1993). Epidemiological studies since 1986 have shown that bamboo rats as *Rhizomys sinensis, Rhizomys pruinosus, Rhizomys sumatrensis* and *Cannomys badius* are hosts of *P. marneffei* (Capponi *et.al.*, 1956; Ajello *et.al.*, 1995; Chariyalertsak *et.al.*, 1996; Denz *et.al.*, 1986; Li, *et.al.*, 1989). Thailand is the greatest endemic area of penicilliosis in AIDs patients (Droughet, 1993). The rare occurrence of penicilliosis in the past and the recent rapid increase in the number of patients coincide with the explosive epidemic of HIV infection in northern Thailand (Supparatpinyo *et.al.*, 1994). Thus *P. marneffei* is one of the medically important dimorphic fungi in this area.

Penicillium marneffei is unique among several hundred species of *Penicillium* because of its thermal dimorphism (Fig.1 and 2). At 25 °C, it is present as mycelia. Detailed descriptions of gross, microscopic, and ultrastructural features of the mycelia and yeast-like phase of *P. marneffei* have been published (Segretain, 1959; Chandler *et.al.*, 1980; Denz *et.al.*, 1986; Garrison and Boyd,1973). When *P. marneffei* is cultured on Sabouraud glucose agar at 25 °C, downy gray - to -white colony is rapidly formed in few days. *Penicillium marneffei* produces a characteristic red pigment that diffuses into the medium. As the conidiophores mature, the surface of the colony appears a blue-green hue. Microscopically, the colony consist of septate branched hyphae with lateral and terminal conidiophores, penicillus is typically divaricate, either symmetrical or asymmetrical, seldom ramified. The conidiophores have basal stipes and terminal verticils of three to five metulae. The metulae bear four to seven phialides, each of which produces long basipetal unbranched chains of conidia. The conidia are oval (2-4 μm x 2-3 μm), often have prominent disjunctors. The typical feature of this pathogenic fungus is the yeast-like phase; unicellular oval or elongated cells (2-3 μm x 2-6.5 μm) which multiply by scissiparity *in vivo* in histiocytes and macrophages (Fig.3) or *in vitro* at 37°C on beer wort agar. The phenomenon of dimorphism occurs in many fungi distributed among the Basidiomycetes, Ascomycetes, Deuteromycetes and Zygomycetes. This is a reversible response to a particular environment and imposed by conditions of growth or available nutrition. When the environmental conditions or nutritional status changes, the fungus reverts to its original morphology and its favored metabolism. Morphogenesis in these fungi

is not essential to their life cycle, but is a response of a change in their habitat. The dimorphic pathogenic fungi are unique in that their ability to invade animal tissue and cause disease is associated with a concomitant morphogenesis to a yeastlike or other "tissue" phase. Thus morphogenesis and disease production are intimately related. There has been great interest in dimorphism as a simple model of cellular morphogenesis (Orlowski, 1991). *Penicillium marneffei* is one of dimorphic fungi, with a parasitic phase consisting of septated yeastlike cells and a saprophytic mycelial phase. It is not known what factors affecting dimorphism of this pathogenic fungi. Since conidium-to-yeast conversion is the essential process for adaptation of the fungus to survive in host tissues and cause disease, this present research is set up to study the environmental factors that induce transformation of *P. marneffei* from conidia to yeastlike cells which will help understanding some biological properties of this pathogenic fungus. Addition to these studies, chitin localization and ultrastructural changes during mycelium-to-yeastlike phase conversion of *P. marneffei* are also examined by Transmission Electron Microscopy (TEM).