Needs Assessment: Current Advances in Melanoma Diagnosis and Treatment

NEEDS OVERVIEW

Skin cancer is the most common type of cancer detected in the United States, with melanoma being its most aggressive form[1]. Melanoma accounts for only 5% of skin cancer diagnoses[1], but is responsible for more than 75% of skin cancer deaths. It is the most common cancer diagnosed among young adults (25-29 years old) in the US[2]. In 2012, approximately 76,250 Americans (44,250 males, 32,000 females) will be diagnosed with melanoma and an additional 55,560 will be diagnosed with melanoma *in situ*[3]. Alarmingly, the incidence of melanoma continues to increase at a rate of about 3.1% per year[4,5]. An estimated 9,180 people (6,060 male, 3,120 female) will die of melanoma[3] in the US in 2012.

Prognosis for early-detected melanoma (while still localized) is favorable, but worsens significantly with delayed diagnosis. The 5-year survival rate for early-diagnosed cases is 98%, but drops to 62% for melanoma that has spread to regional lymph nodes and is only 16% for metastatic melanoma[6]. These statistics underline the importance of early detection, diagnosis and treatment of melanoma. The poor long-term survival rates for metastatic melanoma continue to drive the need for novel developments in the field. This is especially true with regard to better diagnostic tools, new therapies and the identification of prognostic biomarkers to aid individualized treatment.

In addition to the health burden, melanoma carries a significant economic cost. A recent study by Ekwueme et al. estimated an increase of 8.7% in years of potential life lost (YPLL) due to melanoma mortality for the 2000 to 2006 period, compared to only a 2.8% increase for all malignant cancers. The estimated annual cost associated with melanoma mortality in the US was $3.5 billion, or $413,370 lost for every individual who died from melanoma over the 2000-2006 period[7]. In addition, the National Cancer Institute estimates the cost for melanoma care at $2.36 billion for 2010[8], further highlighting the economic burden for society resulting from melanoma.

Pathology and Pathophysiology

Initially, melanoma presents as a pigmented patch of skin - the result of uncontrolled melanocyte growth. This early stage is called radial growth phase. During the radial growth phase, the cancer cells are confined to the epidermis and have not reached the bloodstream. At this stage melanoma is referred to as melanoma *in situ*. Over time, most melanomas enter the invasive radial growth phase, in which cancer cells become capable of spreading radially because of an acquired invasive potential. The next step in melanoma progression is the vertical growth phase. During this phase, malignant cells invade the dermis and develop potential for dermal lymphatic and vascular invasion.

Dysregulation of a number of cell-signaling pathways has been implicated in melanoma. Pathways with high frequency of mutation in melanoma include the Rb and p53[9], and

MAPK pathways[10]. The BRAF V600E mutation is the most common mutation in melanoma cells and accounts for about half of all mutations. These mutations, whether inherited or somatic, lead to deactivation of cell cycle checkpoints, resistance to apoptosis, and increased metastatic potential.