

Abstract

Melanoma is a serious form of skin cancer that can affect people of all ages, including adolescents and young adults (AYAs). Although melanoma is more commonly associated with older adults, younger patients may face unique challenges in detection and treatment. This review examines key factors involved in melanoma development in AYAs, including genetic mutations such as BRAF and NRAS, differences in clinical warning signs, delayed diagnosis, and treatment response. Targeted therapies and immunotherapies have improved treatment options, but resistance and long-term treatment effects remain important concerns. Increasing awareness and expanding age-specific melanoma research may help improve early diagnosis and long-term outcomes for adolescents and young adults.

Introduction

Melanoma is an aggressive form of skin cancer that originates in melanocytes, the pigment-producing cells of the skin. Although melanoma accounts for a small proportion of skin cancer diagnoses, it contributes disproportionately to skin cancer-related deaths. While commonly associated with older adults, melanoma also affects adolescents and young adults (AYAs), generally defined as individuals aged 15–39 years. This review examines the biology, diagnosis, and treatment of melanoma with particular consideration of factors relevant to AYAs.

Methods

A literature review was conducted using PubMed, Google Scholar, and MDPI-published literature. Search terms included “melanoma,” “AYA,” “BRAF mutation,” “NRAS mutation,” “melanoma therapy,” and “melanoma stages.” Peer-reviewed studies were selected based on their relevance to melanoma genetics, epidemiology, diagnosis, and treatment in AYAs. Recent literature was prioritized, with earlier studies included when relevant to established biological or diagnostic concepts. Findings were compared and organized into melanoma biology, genetic alterations, diagnosis in AYAs, and therapeutic strategies.

Melanoma: A Disease For All Ages

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Results

The reviewed literature identified recurrent genetic alterations, including *BRAF* and *NRAS* mutations, as important contributors to melanoma biology and treatment selection. Diagnostic challenges were also identified in younger populations because some melanomas may not display classic clinical warning signs, while lower perceived risk and delayed evaluation of suspicious lesions may further affect detection. Targeted therapies, including BRAF and MEK inhibition, have expanded treatment options for molecularly selected melanomas; however, acquired resistance can limit long-term disease control. Immunotherapy has also produced durable responses in advanced melanoma, although potential long-term treatment effects are particularly relevant for younger patients.

Discussion

The reviewed evidence suggests that melanoma management in AYAs requires consideration of both tumor biology and life stage. Molecular characteristics and clinical presentation may influence diagnosis and treatment, while longer expected survivorship increases the importance of treatment resistance and potential long-term adverse effects. However, limited age-specific evidence makes it difficult to determine how strongly treatment outcomes differ between AYAs and older adults. Additional research focused specifically on AYA populations is needed to better define these differences.

Conclusion

Melanoma can affect patients across the lifespan, but its diagnosis and management in AYAs present important age-specific considerations. Integrating molecular characteristics, clinical presentation, and long-term treatment consequences may support more informed approaches to melanoma care in younger patients.

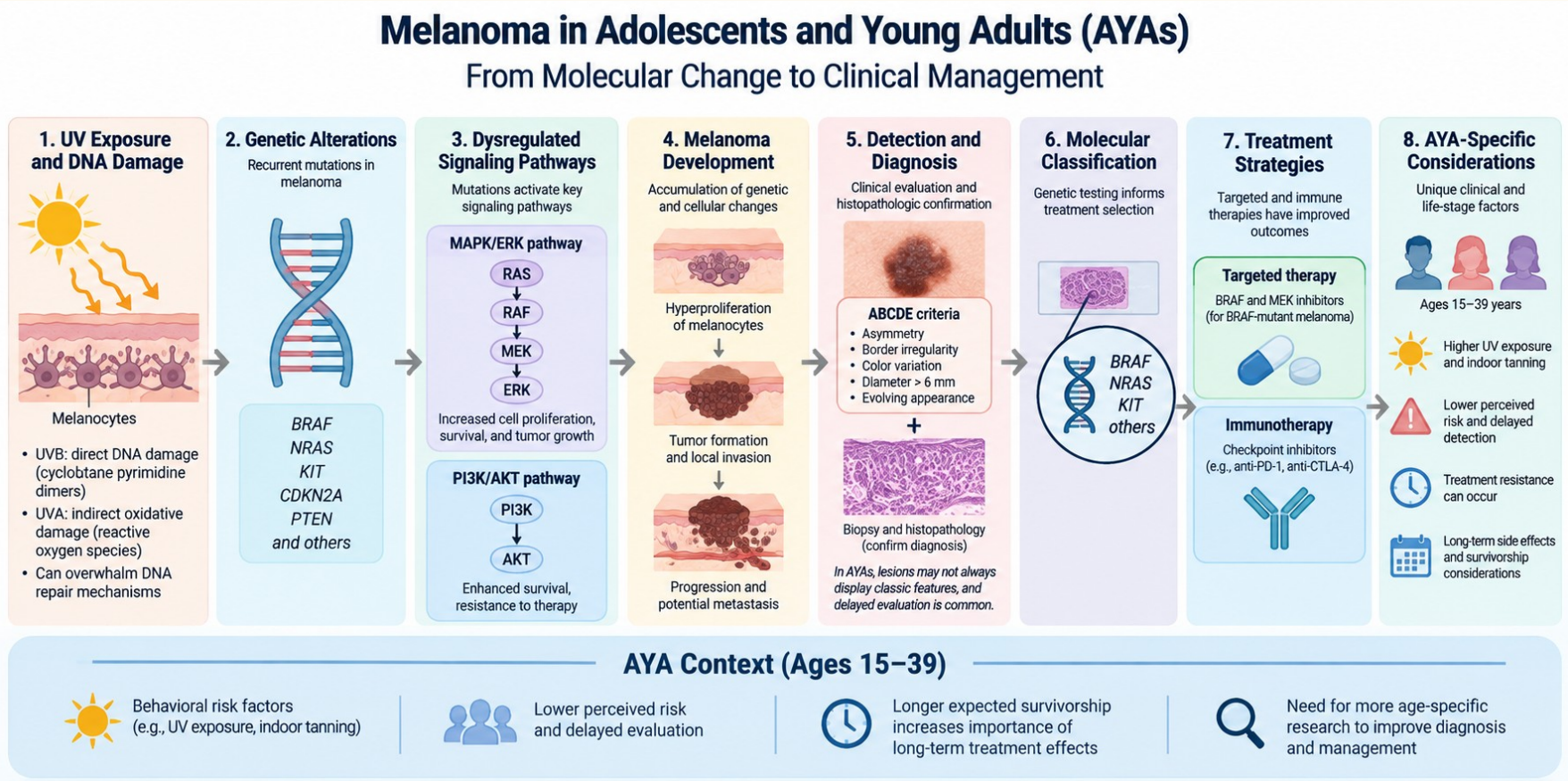


Table 1. Key Genetic Alterations in Melanoma
Common mutations, associated signaling pathways, and clinical relevance in melanoma, with examples of targeted therapies.

Gene	Prevalence (approximate)	Biological Role and Effect in Melanoma	Key Signaling Pathway(s) Affected	Examples of Targeted Therapies and Clinical Relevance
BRAF (most commonly V600E)	~40–60% of cutaneous melanomas	- Encodes a serine/threonine kinase in the MAPK pathway. - Activating mutations (e.g., V600E) lead to constitutive kinase activity, promoting cell proliferation and survival.	BRAF (mutant) ↓ MEK ↓ ERK MAPK/ERK pathway	BRAF inhibitors: vemurafenib, dabrafenib, encorafenib MEK inhibitors: trametinib, cobimetinib, binimetinib (often combined with BRAF inhibitors) Clinical relevance: High response rates in BRAF-mutant melanoma; resistance can develop over time.
NRAS	~15–20% of cutaneous melanomas	- Encodes a small GTPase upstream of the MAPK pathway. - Activating mutations (e.g., Q61R/K/L) lead to continuous signaling and increased cell proliferation and survival.	NRAS (mutant) ↓ MAPK/ERK pathway PI3K/AKT pathway	- No FDA-approved targeted therapy currently. - Investigational approaches include MEK inhibitors, pan-RAF inhibitors, and combination strategies. Clinical relevance: Often associated with more aggressive disease and fewer targeted treatment options.
KIT	~2–5% (more common in acral, mucosal, and chronically sun-damaged melanomas)	- Encodes a receptor tyrosine kinase involved in cell growth, survival, and differentiation. - Activating mutations lead to ligand-independent signaling and tumor growth.	KIT (mutant) ↓ PI3K/AKT pathway Also activates MAPK/ERK pathway	KIT inhibitors: imatinib, nilotinib, dasatinib (in selected patients) Clinical relevance: More frequent in non-UV-driven melanomas; responses can be variable.
CDKN2A	~5–15% (germline mutations in familial melanoma; somatic loss in sporadic cases)	- Encodes tumor suppressor proteins p16INK4A and p14ARF. - Loss of function leads to uncontrolled cell cycle progression and impaired p53-mediated responses.	p16INK4A (loss of function) → CDK4/6 → Rb Cell cycle progression	- No direct targeted therapy; CDK4/6 inhibitors (e.g., palbocicli) under investigation. Clinical relevance: Important in familial melanoma and contributes to cell cycle dysregulation.
PTEN	~5–20% of cutaneous melanomas	- Encodes a lipid phosphatase that negatively regulates the PI3K/AKT pathway. - Loss of function leads to enhanced cell survival, proliferation, and resistance to apoptosis.	PTEN (loss of function) → PI3K → AKT Increased survival and resistance to therapy	- No direct targeted therapy; PI3K/AKT/mTOR inhibitors under investigation. Clinical relevance: Associated with therapy resistance and poor prognosis in some studies.

Note: Prevalence ranges are approximate and may vary by melanoma subtype and study population.
Abbreviations: AKT, protein kinase B; BRAF, B-Raf proto-oncogene; CDK, cyclin-dependent kinase; ERK, extracellular signal-regulated kinase; KIT, receptor tyrosine kinase; MAPK, mitogen-activated protein kinase; MEK, MAPK/ERK kinase; mTOR, mechanistic target of rapamycin; NRAS, neurofiblastoma RAS viral oncogene homolog; PTEN, phosphatase and tensin homolog; Rb, retinoblastoma protein; UV, ultraviolet.