

RESIDENT ROUNDS: PART II

Autosomal Dominant Disorders With Malignant Potential: Board Review

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INTRODUCTION

Our understanding of genodermatoses continues to expand every year with both detailed genetic knowledge and associated clinical findings. It is important to be able to recognize and decipher these complicated diseases in clinical practice. However, remembering this ever-increasing information for the board exam is daunting. We find it helpful to group disorders within a familiar context to generate a frame of reference. This chart illustrates the autosomal dominant disorders with a potential to develop a malignancy. It also includes helpful mnemonics in red below each genetic syndrome and has bolded associated malignancies to assist in recall.

Autosomal Dominant Disorders With Malignant Potential

Genetic Syndrome	Gene	Clinical findings and Malignancies
Nevoid Basal Cell Carcinoma Syndrome Gorlin Syndrome **Vismodegib -> Smoothened receptor**	**PTCH1** (tumor suppressor gene encoding sonic hedgehog)	**BCC's**, palmoplantar pits, milium, EICs, odontogenic cysts, frontal bossing, bifid ribs Neuro: vertebral fusion, calcified falx cerebri, agensis of corpus callosum, medulloblastoma, Ocular: hypertelorism, congenital blindness, cataracts, colobomas, strabismus GU: ovarian fibromas/fibrosarcoma.
Muir-Torre Syndrome **More Oily with Torre**	**MSH2 and MSH1** (DNA mismatch repair genes)	**Sebaceous tumors** (adenomas most common, carcinomas, hyperplasias, epitheliomas, BCC with sebaceous differentiation), KA's, **Colon cancer**, other GI tract, GU, lung, breast and heme malignancies described.
Gardner Syndrome **Birds CHRPE in the Garden**	**APC** gene (tumor suppressor that regulates **B-catenin**)	Epidermoid cysts, CHRPE (Congenital hypertrophy of retinal pigment epithelium), Odontomas GI: hamartomatous polyps, **adenocarcinoma**, desmoid tumors.
Birt-Hogg-Dube Syndrome **Burt hogs follicles**	**BHD** gene (**folliculin**)	Fibrofolliculomas, trichodiscomas, acrochordons. **Renal cell carcinoma.** Pulm: recurrent spontaneous pneumothoraces, lung cysts, bullous emphysema.
Brooke-Speigler Syndrome **Brooke is trichy and cilly**	**CYLD**	Trichoepitheliomas, Cylindromas, ↑ risk for **renal cell carcinoma**.
Rombo **Rambo sweats, has acne scars and BCCs**	Unknown	Milia, atrophoderma vermiculatum (face), normal sweating, **BCCs**

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Genetic Syndrome	**Gene**	**Clinical findings and Malignancies**
Multiple Hamartoma Syndrome Cowden Syndrome **Tricholemoomoo's in Cowden**	**PTEN**, a tumor suppressor	Facial tricholemmomas, oral papillomas (cobblestone), punctate keratsoes on palms/soles Breast: fibrocystic disease, adenocarcinoma. Thyroid: goiter, adenomas, **follicular adenocarcinoma**. GI: hamartomatous polyps. GU: Ovarian cysts.
Peutz-Jeghers Syndrome Periorificial lentiginosis **Peutz on your lip STK**	**STK11** (serine/threonine kinase 11)	Pigmented macules, brown to black in color, on periorificial skin, lips, buccal mucosa, digits, nails, palms, soles, any mucosal surface (fade by puberty); GI: hamartomatous polyps, adenocarcinoma. **Breast/ ovarian cancers**.
Familial multiple leiomyomatosis **Painful muscles make you Fuming mad**	**Fumarate hydratase**	Leiomyomas (cutaneous and uterine), ↑ **renal cell cancer**
Ferguson-Smith syndrome **Fergie erupts in childhood**	**TGFBR1** gene	Multiple eruptive **KAs** during childhood and adolescence, recur later. Face and extremities most common. Gryzbowski syndrome: eruptive **KAs** adults
Multiple Endocrine Neoplasia Type I Werner's Syndrome	**Menin**	**P**arathyroid, **P**ancreatic, **P**ituitary **cancers** Angiofibromas, CALMs, collagenomas, lipomas, gingival macules
Multiple Endocrine Neoplasia Type IIa Sipple's Syndrome	**RET** proto-oncogene	**P**arathyroid cancer, **P**heocromocytoma, **Medullary thyroid cancer** ↑ incidence familial macular or lichen amyloidosis
Multiple Endocrine Neoplasia Type IIb Multiple mucosal neuroma syndrome	**RET** proto-oncogene	**P**heochromocytoma, **Medullary thyroid cancer** Mucosal neuromas on tongue and lips, thickened "blubbery" lips, thickened, everted upper lids, corneal nerve thickening, marfanoid habitus, megacolon.

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