From the Editor

Endocrine Cancers: Defying the Paradigms

Endocrine cancers, studied for the boards and then largely forgotten by medical oncologists, comprise a set of rare but very interesting tumors with a diverse clinical spectrum. Few tumors are more aggressive than adrenocortical cancer or more lethal than anaplastic thyroid cancer. And few are more indolent than pituitary tumors, parathyroid tumors, or papillary thyroid tumors, where a subset is now proposed to be reclassified as benign. Endocrine cancers are often difficult to differentiate from their benign counterparts; their ability to synthesize hormones underscores their differentiated phenotypes. That so often they look and behave "normal" is consistent with their low mutation burden, which is markedly lower than lung, bladder, and upper gastrointestinal cancers. Even poorly differentiated thyroid cancer has a low mutation burden. Despite their low number of mutations, as shown in data derived from The Cancer Genome Atlas (TCGA) in Fig. 1, many endocrine cancers harbor common "driver mutations" —*BRAF*, *RAS*, *RET*, *SDHx*, and *PRKARIA*. But counterintuitively, targeted therapeutics have not shown improved overall survival in phase III placebo-controlled clinical trials. It is these failures that inspire further studies to understand this refractoriness and also to develop targeted therapeutics for adrenocortical cancer, malignant pheochromocytomas, poorly differentiated and anaplastic thyroid cancers, and pancreatic neuroendocrine tumors. The experts gathered for this *CCR Focus* with Guest Editor Sam Wells offer us much to think about in the diagnosis and management of this important group of neoplasms, and much to inform our thinking elsewhere in oncology.

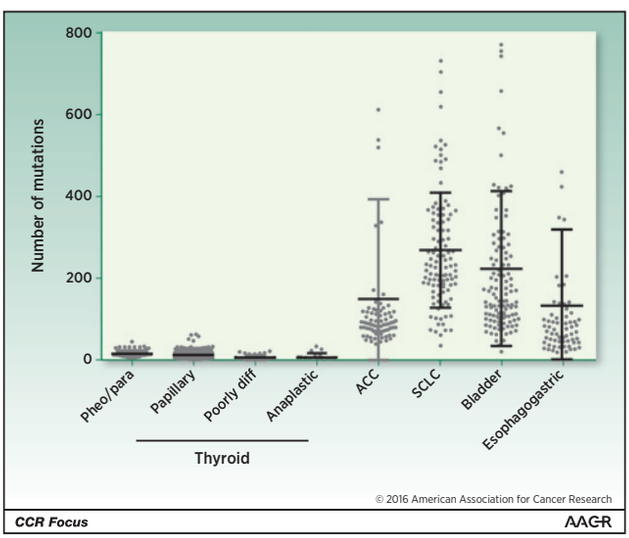

Figure 1.
Mutation burden from TCGA BioPortal. Graphs showing the mutation counts for datasets of tumors sequenced and uploaded to the website. The results in the figure are based upon TCGA data (1) and downloaded from cBioPortal (2–4). ACC, adrenocortical cancer; Para, paraganglioma; Pheo, pheochromocytoma; Poorly diff, poorly differentiated; SCLC, small cell lung cancer.

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See all articles in this *CCR Focus* section, "Endocrine Cancers: Revising Paradigms."

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