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ORIGINAL ARTICLE

Cutaneous carcinosarcoma: further insights into its mutational landscape through massive parallel genome sequencing

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Abstract Cutaneous carcinosarcoma (CCS) is an extraordinarily rare neoplasm with a biphasic morphological pattern exhibiting both epithelial and sarcomatoid components. Although its histogenesis and biological aspects remain poorly understood, previous studies have postulated that this tumor may arise from single cancer stem cells which subsequently differentiate into distinct tumor lineages. In this study, we explored a wide array of mutational hot spot regions, through high-depth next-generation sequencing of 47 cancer-associated genes in order to assess the mutational landscape of these tumors and investigate whether the epithelial and mesenchymal components shared the same genetic signatures. Results from this study confirm that despite their striking phenotypic differences, both elements of this infrequent tumor indeed share a common clonal origin. Additionally, CCS appears to embrace a heterogeneous spectrum with specific underlying molecular signatures correlating with the defining epithelial morphotype, with those carcinosarcomas exhibiting a squamous cell carcinoma epithelial component exhibiting diverse point mutations and deletions in the *TP53* gene, and those with a basal cell carcinoma morphotype revealing a more complex mutational landscape involving several genes. Also, the fact that our findings involve several targetable gene pathways suggests that the underlying molecular events driving the pathogenesis of CCS may represent future potential targets for personalized therapies.

Keywords Carcinosarcoma · Cutaneous · Mutations · Next-generation sequencing · Stem cells · Histogenesis

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Introduction

Originally described by Dawson in 1972, primary cutaneous carcinosarcomas are exceedingly rare skin tumors with around 70 cases reported to date in the English literature [1–3]. Cutaneous carcinosarcomas (CCSs) are biphenotypic tumors, which embrace a heterogenous spectrum of morphotypes characterized by an intimate admixture of epithelial and mesenchymal components with varying degrees of differentiation amongst both elements [4, 5]. The epithelial component can include squamous cell carcinoma, basal cell carcinoma, basal cell carcinoma with focal squamous differentiation, as well as malignant adnexal morphological features [5–8]. On the other hand, the sarcomatous component may be composed of spindle and pleomorphic cells with marked atypia as well as by heterologous elements with chondroblastic and osteoblastic differentiation [4, 5, 9–13]. Currently, literature concerning the molecular events underlying CCS is unavailable. Previous molecular analysis of these histological components in other organs has