1. *CYLD* gene

1.7 Summary

Our team discovered 19 new germinal mutations (22% of all known), with author participating on finding of seven of them. Particularly interesting is the discovery of new intronic mutation of *CYLD* gene and characterization of molecular biologic processes causing inactivation of the gene. Author also confirmed presence of LOH being the most frequent second inactivating hit. At the same time author found a group of patients with BSS/MFT phenotype carrying no mutation of CYLD gene suggesting that there might exist another gene participating in BSS/MFT pathogenesis. Furthermore genotype-phenotype analysis was performed resulting in no significant correlation.

2. Mismatch repair genes *hMLH1, hMSH2, hMSH6*

2.9 Summary

In this study we have analyzed one patient with Muir–Torre syndrome (MTS) phenotype for causal mutation in mismatch repair (MMR) genes. Most patients with MTS carry mutations in *MSH2* and *MLH1* gene. Germline mutations in *MSH6* are extremely rare, with only 3 cases reported thus far. Here we have described a germline mutation in *MSH6* gene in three members of one family. This greatly extends previously published group of patients with MTS syndrome carrying mutation in *MSH6* gene.

3. *PRKAR1A* gene

3.7 Summary

In this study we have investigated patient with Carney complex for a germline mutation of the *PRKAR1A* gene. Carney complex patients carry alterations of the *PRKAR1A* gene in at least 70% of cases. This studied patient belongs to this group, because a causal frame shift mutation in exon 6 of the *PRKAR1A* gene was found in him.

4. *CTNNB1*gene

4.7 Summary

In our study we have performed mutation analysis of part of the *CTNNB1* gene in 89 cutaneous adnexal tumours. We have proven that mutations of this gene are present mainly in tumors with follicular differentiation and mostly with matrical differentiation. Rare examples of trichoblastoma may also harbor this mutation. Our study broadens the spectrum of cutaneous adnexal tumors harboring *CTNNB1* mutations arising from the activation of Wnt/wingless signal pathway.

5. *TP53* gene

5.6 Summary

In this study we have performed mutation analysis of TP53 in 12 of 15 malignant transformed, sporadic or BSS asociated lesions. Samples included cylindromas, spiradenomas and spiradonecylindromas. Even though high precentage of samples was imunohistochemically (IHC) p53 positive, which often suggests presence of mutation in

this gene in neoplastic tissue, only one sample showed mutation in TP53 gene. This shows that as opposed to IHC, mutation analysis of TP53 does not contribute to distinguish malignant cylindromas, spiradenomas and spiradonecylindromas from benign ones.

5.13 Summary

As in the above mentioned study mutation analysis of *TP53* gene was performed here in 9 of the total 14 specimens of hidradenocarcinoma studied. *TP53* mutation was found in two samples. One of the samples was imunohistochemicaly (IHC) p53 positive and the other was negative. As in the previous study IHC result does not correlate with mutation analysis however the frequency of the mutations is similar to other cutaneous tumours.

6. *HER2/neu* gene

6.7 Summary

In a study of cutaneous hidrodenocarcinoma IHC analysis for c-erbB2 (HER2) protein was performed in 8 specimens from 5 cases. Three specimens which showed borderline results (IHC 2+) were all subsequently proved negative for *Her2/neu* gene amplification by FISH. According to our study this alteration doesn´t contribute to the origin and progress of cutaneous hidrodenocarcinoma.

7. *CRTC1* a *MAML2* genes, translocation t(11;19)(CRTC1/MAML2)

7.7 Summary

Presence of translocation t(11;19), a characteristic sign for a part of hidradenomas was analyzed for the first time in the study of cutaneous hidradenocarcinomas. This translocation was found in 14% of cases of hidradenocarcinomas, which suggests that at least some part of this group of tumours originates and progresses as a result of this chromosomal rearrangement.