Liver cancer—also called hepatocellular carcinoma (HCC)—is the most frequent primary liver cancer in humans. As of today, it is mainly induced by chronic virus infections such as Hepatitis B and C viruses, which induce chronic hepatitis and fibrosis, the two most important conditions predisposing towards HCC development. Besides, chronic alcohol or drug consumption contributes to chronic liver injury and HCC development. Of note, in industrialized countries virus infections have recently been outcompeted by a high-fat and high-sugar diet as the most important etiology for HCC development in humans—now representing the fastest growing cancer in the USA as of today. It is believed that soon also in Europe high-fat diet caused HCC will become the fastest growing cancer. Today more than 800,000 people die every year due to cancer; however, despite a great research effort in the last 20 years, no efficient curative therapy is available at the moment. It has turned out that various subtypes of HCC exist in humans, complicating the therapy for HCC patients in general, and leading to the need for therapies of stratified patient cohorts as the variability of HCC phenotypes (6 different subtypes exist as of today) influences the responsiveness to treatment. Thus, it is important to dissect and characterize the various HCC subtypes in humans as well as in mouse models to identify the sub-cohorts that are responsive to particular therapies. One step to do so is the characterization of HCC nodules
on genetic level. Here, we describe a protocol to characterize individual HCC nodules on genomic level, enabling to stratify the respective liver carcinoma and select them for a more targeted therapy.