Chapter 1

Experiments and Results

This section will contain the results from the experiments.

1.1 Litterature search

The litterature search yielded 123 studies of interest. Of these 25 had raw microRNA public. For the other studies, we sent an email requesting the raw miRNA data. However, only one such dataset were recieved, leading to an overall 26 datasets that are analyzed in this project ([Asakura et al., 2020], [Bianchi et al., 2011], [Boeri et al., 2011], [Chen et al., 2019], [Duan et al., 2021], [**?**], [Halvorsen et al., 2016], [Jin et al., 2017], [Keller et al., 2009], [Keller et al., 2014], [Keller et al., 2020], [Kryczka et al., 2021], [Leidinger et al., 2011], [Leidinger et al., 2014], [Leidinger et al., 2015b], [Leidinger et al., 2015a], [Li et al., 2017], [Marzi et al., 2016], [Nigita et al., 2018], [Patnaik et al., 2012], [Patnaik et al., 2017], [Qu et al., 2017], [Reis et al., 2020], [Wozniak et al., 2015], [**?**], [Zaporozhchenko et al., 2018]).

The distribution of technologies in these different studies are visualized in Figure **??**. The number of samples are

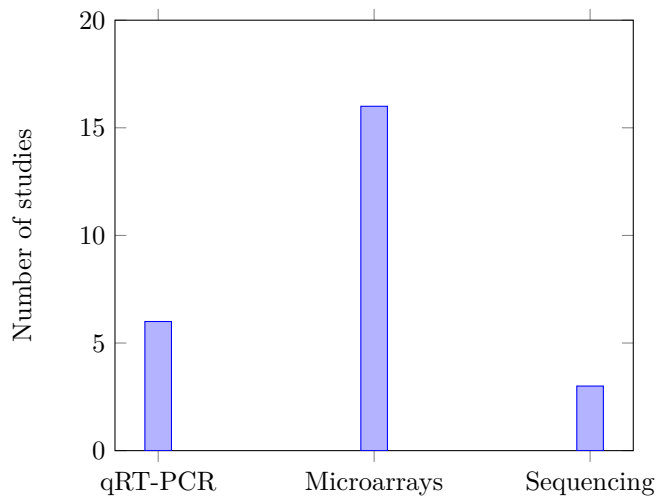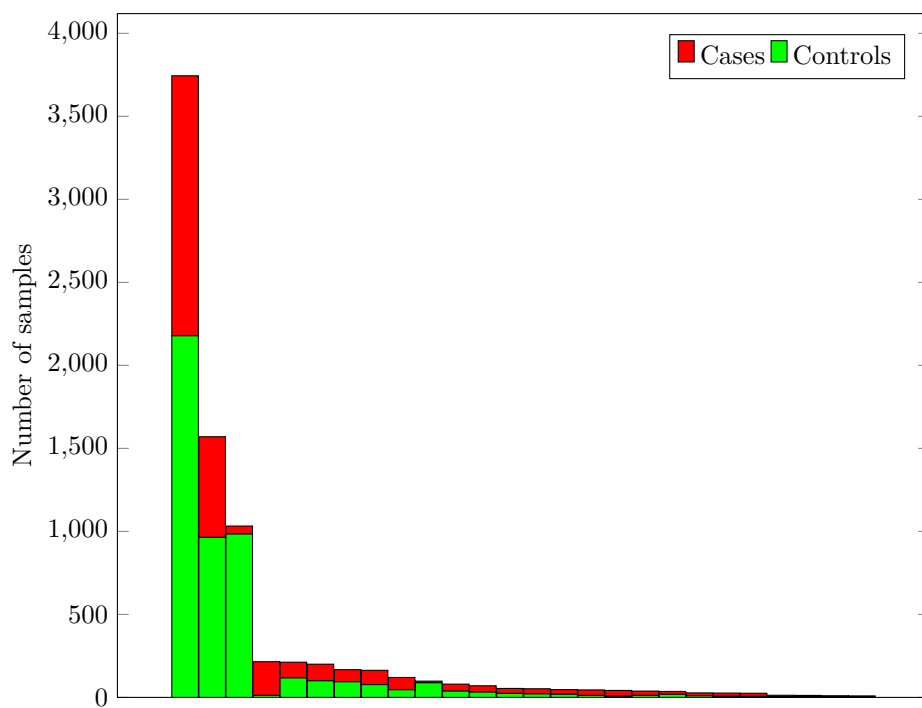## 1.2 Processing the datasets

Figure 1.1: Number of studies of each type

Bibliography

Asakura, K., Kadota, T., Matsuzaki, J., Yoshida, Y., Yamamoto, Y., Nakagawa, K., Takizawa, S., Aoki, Y., Nakamura, E., Miura, J., Sakamoto, H., Kato, K., Watanabe, S.-i., and Ochiya, T. (2020). A miRNA-based diagnostic model predicts resectable lung cancer in humans with high accuracy. *Communications Biology*, 3(1):1–9.

Bianchi, F., Nicassio, F., Marzi, M., Belloni, E., Dall'Olio, V., Bernard, L., Pelosi, G., Maisonneuve, P., Veronesi, G., and Di Fiore, P. P. (2011). A serum circulating miRNA diagnostic test to identify asymptomatic high-risk individuals with early stage lung cancer. *EMBO Molecular Medicine*, 3(8):495–503.

Boeri, M., Verri, C., Conte, D., Roz, L., Modena, P., Facchinetti, F., Calabrò, E., Croce, C. M., Pastorino, U., and Sozzi, G. (2011). MicroRNA signatures in tissues and plasma predict development and prognosis of computed tomography detected lung cancer. *Proceedings of the National Academy of Sciences*, 108(9):3713–3718.

Chen, X., Jin, Y., and Feng, Y. (2019). Evaluation of Plasma Extracellular Vesicle MicroRNA Signatures for Lung Adenocarcinoma and Granuloma With Monte-Carlo Feature Selection Method. *Frontiers in Genetics*, 10:367.

Duan, X., Qiao, S., Li, D., Li, S., Zheng, Z., Wang, Q., and Zhu, X. (2021). Circulating miRNAs in Serum as Biomarkers for Early Diagnosis of Non-small Cell Lung Cancer. *Frontiers in Genetics*, 12:987.

Halvorsen, A. R., Bjaanæs, M., LeBlanc, M., Holm, A. M., Bolstad, N., Rubio, L., Peñalver, J. C., Cervera, J., Mojarrieta, J. C., López-Guerrero, J. A., Brustugun, O. T., and Helland, Å. (2016). A unique set of 6 circulating microRNAs for early detection of non-small cell lung cancer. *Oncotarget*, 7(24):37250–37259.

Jin, X., Chen, Y., Chen, H., Fei, S., Chen, D., Cai, X., Liu, L., Lin, B., Su, H., Zhao, L., Su, M., Pan, H., Shen, L., Xie, D., and Xie, C. (2017). Evaluation

of Tumor-Derived Exosomal miRNA as Potential Diagnostic Biomarkers for Early-Stage Non–Small Cell Lung Cancer Using Next-Generation Sequencing. *Clinical Cancer Research*, 23(17):5311–5319.

Keller, A., Fehlmann, T., Backes, C., Kern, F., Gislefoss, R., Langseth, H., Rounge, T. B., Ludwig, N., and Meese, E. (2020). Competitive learning suggests circulating miRNA profiles for cancers decades prior to diagnosis. *RNA Biology*, 17(10):1416–1426.

Keller, A., Leidinger, P., Borries, A., Wendschlag, A., Wucherpfennig, F., Scheffler, M., Huwer, H., Lenhof, H.-P., and Meese, E. (2009). miRNAs in lung cancer - Studying complex fingerprints in patient's blood cells by microarray experiments. *BMC Cancer*, 9(1):353.

Keller, A., Leidinger, P., Vogel, B., Backes, C., ElSharawy, A., Galata, V., Mueller, S. C., Marquart, S., Schrauder, M. G., Strick, R., Bauer, A., Wischhusen, J., Beier, M., Kohlhaas, J., Katus, H. A., Hoheisel, J., Franke, A., Meder, B., and Meese, E. (2014). miRNAs can be generally associated with human pathologies as exemplified for miR-144*. *BMC Medicine*, 12(1):224.

Kryczka, J., Migdalska-Sęk, M., Kordiak, J., Kiszałkiewicz, J. M., Pastuszak-Lewandoska, D., Antczak, A., and Brzeziańska-Lasota, E. (2021). Serum Extracellular Vesicle-Derived miRNAs in Patients with Non-Small Cell Lung Cancer—Search for Non-Invasive Diagnostic Biomarkers. *Diagnostics*, 11(3):425.

Leidinger, P., Backes, C., Dahmke, I. N., Galata, V., Huwer, H., Stehle, I., Bals, R., Keller, A., and Meese, E. (2014). What makes a blood cell based miRNA expression pattern disease specific? - A miRNome analysis of blood cell subsets in lung cancer patients and healthy controls. *Oncotarget*, 5(19):9484–9497.

Leidinger, P., Brefort, T., Backes, C., Krapp, M., Galata, V., Beier, M., Kohlhaas, J., Huwer, H., Meese, E., and Keller, A. (2015a). High-throughput qRT-PCR validation of blood microRNAs in non-small cell lung cancer. *Oncotarget*, 7(4):4611–4623.

Leidinger, P., Galata, V., Backes, C., Stähler, C., Rheinheimer, S., Huwer, H., Meese, E., and Keller, A. (2015b). Longitudinal study on circulating miRNAs in patients after lung cancer resection. *Oncotarget*, 6(18):16674–16685.

Leidinger, P., Keller, A., Borries, A., Huwer, H., Rohling, M., Huebers, J., Lenhof, H.-P., and Meese, E. (2011). Specific peripheral miRNA profiles for distinguishing lung cancer from COPD. *Lung Cancer*, 74(1):41–47.

Li, L.-L., Qu, L.-L., Fu, H.-J., Zheng, X.-F., Tang, C.-H., Li, X.-Y., Chen, J., Wang, W.-X., Yang, S.-X., Wang, L., Zhao, G.-H., Lv, P.-P., Zhang, M., Lei,

Y.-Y., Qin, H.-F., Wang, H., Gao, H.-J., and Liu, X.-Q. (2017). Circulating microRNAs as novel biomarkers of ALK-positive non-small cell lung cancer and predictors of response to crizotinib therapy. *Oncotarget*, 8(28):45399–45414.

Marzi, M. J., Montani, F., Carletti, R. M., Dezi, F., Dama, E., Bonizzi, G., Sandri, M. T., Rampinelli, C., Bellomi, M., Maisonneuve, P., Spaggiari, L., Veronesi, G., Bianchi, F., Di Fiore, P. P., and Nicassio, F. (2016). Optimization and Standardization of Circulating MicroRNA Detection for Clinical Application: The miR-Test Case. *Clinical Chemistry*, 62(5):743–754.

Nigita, G., Distefano, R., Veneziano, D., Romano, G., Rahman, M., Wang, K., Pass, H., Croce, C. M., Acunzo, M., and Nana-Sinkam, P. (2018). Tissue and exosomal miRNA editing in Non-Small Cell Lung Cancer. *Scientific Reports*, 8(1):10222.

Patnaik, S. K., Kannisto, E. D., Mallick, R., Vachani, A., and Yendamuri, S. (2017). Whole blood microRNA expression may not be useful for screening non-small cell lung cancer. *PLOS ONE*, 12(7):e0181926.

Patnaik, S. K., Yendamuri, S., Kannisto, E., Kucharczuk, J. C., Singhal, S., and Vachani, A. (2012). MicroRNA Expression Profiles of Whole Blood in Lung Adenocarcinoma. *PLOS ONE*, 7(9):e46045.

Qu, L., Li, L., Zheng, X., Fu, H., Tang, C., Qin, H., Li, X., Wang, H., Li, J., Wang, W., Yang, S., Wang, L., Zhao, G., Lv, P., Lei, Y., Zhang, M., Gao, H., Song, S., and Liu, X. (2017). Circulating plasma microRNAs as potential markers to identify EGFR mutation status and to monitor epidermal growth factor receptor-tyrosine kinase inhibitor treatment in patients with advanced non-small cell lung cancer. *Oncotarget*, 8(28):45807–45824.

Reis, P. P., Drigo, S. A., Carvalho, R. F., Lopez Lapa, R. M., Felix, T. F., Patel, D., Cheng, D., Pintilie, M., Liu, G., and Tsao, M.-S. (2020). Circulating miR-16-5p, miR-92a-3p, and miR-451a in Plasma from Lung Cancer Patients: Potential Application in Early Detection and a Regulatory Role in Tumorigenesis Pathways. *Cancers*, 12(8):2071.

Wozniak, M. B., Scelo, G., Muller, D. C., Mukeria, A., Zaridze, D., and Brennan, P. (2015). Circulating MicroRNAs as Non-Invasive Biomarkers for Early Detection of Non-Small-Cell Lung Cancer. *PLOS ONE*, 10(5):e0125026.

Zaporozhchenko, I. A., Morozkin, E. S., Ponomaryova, A. A., Rykova, E. Y., Cherdyntseva, N. V., Zheravin, A. A., Pashkovskaya, O. A., Pokushalov, E. A., Vlassov, V. V., and Laktionov, P. P. (2018). Profiling of 179 miRNA Expression in Blood Plasma of Lung Cancer Patients and Cancer-Free Individuals. *Scientific Reports*, 8(1):6348.