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Using microRNAs to understand cancer biology

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MicroRNAs are non-coding RNA species that have a crucial role in growth, development, and cell death and differentiation. Since the initial groundbreaking discovery that these tiny cellular shepherds were aberrantly expressed in cancer,¹ there has been an explosion in the study of microRNAs in cancer risk, development, biology, and outcome. As evidence grows that microRNAs are aberrantly expressed in all cancer types, it is becoming clear that the microRNAs most important in each tissue, and thus each cancer type, are not the same. Identifying the microRNAs relevant for each tumour type is crucial not only for assisting the pathological classification of tumours, but also for defining biological behaviour and ultimately tailoring treatment to each cancer type and each patient with cancer.

Currently cancer treatment is guided by the paradigm that cancers arising in the same organ should be treated with the same treatment regimen. Although it is recognised that different histological subclasses of tumours arising in the same organ might be biologically different, there are few biologically based markers available to both identify and understand these differences. While in some tumour types unique therapies are now available for different subtypes of cancers, such as in breast cancer, this has not been the case for most cancer types. This area is in fact a new and important application for microRNAs in cancer, as Ueda and colleagues show in *The Lancet Oncology*.² In their paper the authors are able to prove that microRNA signatures can differentiate diffuse and intestinal histological subtypes of gastric cancer. This is important, as these tumours have different biological behaviour, and different microRNA signatures should, and in fact do, reflect this. The fact that different subtypes of gastric cancer can be classified by microRNA signatures is an important indicator of their unique biology, and the potential for microRNAs to be used in such biological classification within tumour types has not been previously appreciated in microRNA-profiling studies. As our understanding of these biological differences evolves, and more targeted therapies are defined, these microRNA-based classifications will significantly affect cancer treatment.

Another important area in which microRNAs have proven to be extremely powerful is the prediction of tumour outcome.³ This type of information is crucial for patients and physicians, as it enables doctors to determine the best therapy. Knowing that a patient has a more aggressive tumour and a poor prognosis will give doctors the confidence to treat them aggressively, whereas patients with less aggressive tumours and a good prognosis might be able to avoid cytotoxic therapy and its side-effects. Ueda and colleagues show that microRNA profiling of gastric tumours enables this type of risk stratification, as they identify microRNA expression patterns that predict outcome for patients with gastric cancer. This type of study needs to be done for every cancer type. These types of study are significant steps toward personalised risk stratification, and are crucial in an era where the

use of expensive adjuvant therapy is being challenged. One can imagine that an upfront assessment of a tumour's microRNA signature, and therefore its biology, will soon be adopted as the first step taken by the treating oncologist.

While there is considerable work still to be done to understand how microRNA disruption initially occurs, how tumours maintain these abnormal microRNA signatures, and how microRNA manipulation can be successfully done to reverse these abnormalities, microRNAs are proving to be enormously powerful in aiding the understanding of cancer biology. Studies such as that by Ueda and colleagues offer hope to patients with cancer that in the future they will be offered truly tailored treatment, based on the unique biology of their tumour as defined by microRNAs.

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References

1. Calin GA, Dumitru CD, Shimizu M, et al. Frequent deletions and down-regulation of micro- RNA genes miR15 and miR16 at 13q14 in chronic lymphocytic leukemia. *Proc Natl Acad Sci USA*. 2002; 99:15524–29. [PubMed: 12434020]
2. Ueda T, Volinia S, Okumura H, et al. Relation between microRNA expression and progression and prognosis of gastric cancer: a microRNA expression analysis. *Lancet Oncol*. 2009; published online Dec 21. doi: 10.1016/S1470-2045(09)70343-2
3. Takamizawa J, Konishi H, Yanagisawa K, et al. Reduced expression of the let-7 microRNAs in human lung cancers in association with shortened postoperative survival. *Cancer Res*. 2004; 64:3753–56. [PubMed: 15172979]