Histogenesis And Morphogenesis In Planarian Regeneration Monographs In Developmental Biology Vol 11

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planarian regeneration deals with regeneration problems including embryogenesis and morphogenesis the book compares the principles involved in the regeneration processes with those in ontogenesis from the egg the author also reviews the works of thomas h morgan and charles m child which became the basis for systematic scientific investigation of regeneration the head regenerates vigorously with a faster rate behind the eyes then at various levels along the longitudinal axis of the planarian body a time graded regeneration includes inhibitory forces and some genetic codes that determine such rate the time graded field has been proven by transplantation experiments the author addresses the morphological structure to which biochemical factors or processes determine the different rate of regeneration he notes that the nervous

system conforms to these processes as shown by studies of lender and klein 1961 the author suggests that the study of regeneration in planarians should involve time considerations quantitatively to explain some substance if any from the nervous system that activates the cytoplasm of neoblasts and then the genome this book will prove valuable for zoologists and researchers in genetics biochemistry or molecular biology

there is an unbreakable link between shape and function in biology the architecture of cells tissues and organisms that have evolved adapting to the world around them translate into specific functional outcomes self organization is an adaptive non linear and dynamic process where diverse ordered patterns emerge from an initially disordered and noisy state through local interactions between the elements of a system this can lead to the fascinating biological diversity and functional complexity in such systems unwavering storms on the surface of jupiter patterns on the wing of a butterfly a regenerating planarian eye development of a neuronal circuit in the human brain can all be studied systematically using the conceptual tools derived from the field of self organization here i sought to address a central but understudied problem in animal regeneration how do regenerative progenitors organize into complex replacement structures in the context of adult anatomy i used the planarians as a system for studying regenerative progenitors and focused on eye regeneration to elucidate the mechanisms i found that self organization has a major role in determining the behavior of regenerative progenitors this work revealed three properties that govern regenerative progenitor behavior and these three properties in concert explain many previously mysterious aspects of how regeneration works i self organization ii an extrinsic migratory target for progenitors and iii a broad progenitor specification zone that allows progenitors to be targeted into self organizing systems even if they are transiently in incorrect locations during the process of regeneration these components yield a model with broad explanatory and predictive power as an example we were able to generate wild type animals with 3 4 or

5 eyes instead of 2 by simple manipulations of the system using the model developed remarkably the extra eyes were stably maintained throughout the life of the animal resulting in wild type animals with an alternative and stable anatomical state this model prominently incorporates self organizing principles which have been little explored in regeneration the new conceptual model with broad explanatory power allowed us to address some of the fundamental previous mysteries of regeneration

this volume explores the various facets of planaria as a biomedical model system and discusses techniques used to study the fascinating biology of these animals the chapters in this book are divided into two parts part one looks at the biodiversity of planarian species the molecular orchestration of regeneration ecology of planarians in their natural habitats and their history as lab models part two talks about experimental protocols for studying planarians ranging from the establishment of a planarian research colony to rna and dna extraction techniques all the way to single stem cell transplantations or metabolomics analysis written in the highly successful methods in molecular biology series format chapters include introductions to their respective topics lists of the necessary materials and reagents step by step readily reproducible laboratory protocols and tips on troubleshooting and avoiding known pitfalls comprehensive and cutting edge planarian regeneration methods and protocols is a valuable resource for both newcomers to the field and experts within established planarian laboratories

some animals have incredible regenerative abilities which kept researchers fascinating during decades how these animals are able to regenerate missing parts and restore damaged tissues can give researchers insights in the regenerative medicine field here we use the planarian schmidtea mediterranea specie which is able to fully regenerate every missing part to deeper understand the regeneration and the tissue renewal processes

both processes share several mechanisms which are essentials for their correct development in this thesis we described some aspect of the balance between proliferation and apoptosis the stem cell differentiation and the positional instructions required all of them to properly regenerate any structure and produce the tissue turn over required during the normal homeostasis of the animals to study the balance between proliferation and apoptosis we were focused in the description of krüppel like factor 10 11 which in other organisms is also involved in these mechanisms here we show that klf10 11 is required for the proper regulation of proliferation and apoptosis in regeneration and that they are essential for the correct remodelling of the organism structures probably downstream c jun n terminal kinase on the other hand we have been focused on the study of the transcriptional complex nuclear factor y in order to understand its role during differentiation events in planarian we have shown that planarian nf y is essential for regeneration and homeostasis and that its inhibition generates neoblast accumulation and absence of epidermal progenitors which demonstrates that nf y is involved in the early differentiation of epidermal lineage progenitors finally the positional instructions which are essential for the correct positioning of cells and organs during regeneration and homeostasis have been studied here we have been focused in the control of the medio lateral organization of the central nervous system in planarian where wnt5 and slit play an essential role wnt5 slit and their receptors create a self regulatory system to establish the medio lateral pattern in planarians which guide the cns to be positioned in this axis tdx

this dissertation the role of extracellular matrix in planarian regeneration by yun shen ⊠⊠ was obtained from the university of hong kong pokfulam hong kong and is being sold pursuant to creative commons attribution 3 0 hong kong license the content of this dissertation has not been altered in any way we have altered the formatting in order to facilitate the ease of printing and reading of the dissertation all rights not granted by the

above license are retained by the author abstract extracellular matrix ecm is an important niche component and its role in stem cell biology is well recognized however the role of ecm in tissue regeneration is not well understood recent findings suggest ecm synthesis and it s remodeling by matrix metalloproteinases act as key regulatory systems in wound repair and tissue regeneration there are many animals with regenerative potentials such as hydra planarian and salamander a common process in their tissue regeneration is the formation of a blastema the planarians however have the most effective regenerative potential being able to regenerate any missing parts of the organism and are considered immortal under the knife this regenerative feat is thought to be by its large population of stem cells here i use the planarian as a model system studying the dynamic protein expression changes in the earliest events in tissue regeneration to gain insights into the role of ecm in regeneration using a novel type of time lapse microscopy i showed that the blastema in the first 2 days of regeneration appears homogenous containing mostly undifferentiated stem cells recruited from the old tissue in contrast major morphological changes could be observed between days 3 and 4 consistent with the rapid proliferation and or differentiation of stem cells coordinated with reorganization of tissue components proteome expression profiling of the blastema during the first 4 days of regeneration was performed that showed many distinctive expression pattern of proteins key changes included components of wnt signaling pathways which were up regulated in late stages of tail blastema consistent with their roles in promoting tail formation in contrast negative regulators of wnt were up regulated in the regenerating head ensuring the regeneration of anterior structures interestingly many ecm proteins were also dynamically expressed suggesting the regulation of matrix assembly and remodeling is important for regeneration expression analysis of two collagen chains dj col1 and dj col2 showed that they were co expressed with piwi expressing stem cells in intact planarians however in blastema their co expression with piwi positive cells was delinked knock down of dj col1 and dj col2 by rnai in amputated planarians resulted in faster regeneration quantitative analysis

indicated there was a general increase in the number of piwiexpressing stem cells following rnai treatment consistent with a negative effect on stem cell function and regeneration for these collagen chain proteins expression of two putative matrilysins dj mmp1 and dj mmp2 were found to be around the pharynx region in the intact planarian in regeneration their expressions decreased in regenerating blastema however the typical expression patterns of these genes were quickly reconstituted in the old tissue consist with a role of these metalloproteinases mmps in remodeling the old tissue for integration with the new tissues or for the maintenance proportion and function of all the organs this study has provided the first insight into the role of ecm and mmps in the regenerative processes of planarians additional analyses of other collagen chain proteins and more detailed functional studies are needed to better define the precise role of ecm molecules in regeneration doi 10 5353 th b5328027 subjects extracellular matrix

how animals establish and maintain the sizes of myriad tissues and organs in tight proportion to one another is a fundamental question of developmental biology planarian flatworms regenerate from diverse injuries in each case precisely restoring body parts to their appropriate proportions underlying this ability is a pluripotent population of dividing cells called neoblasts which are required for homeostatic maintenance and regeneration of all planarian tissues whether neoblasts restore proportion by sensing and responding to the presence or absence of specific tissues during regeneration is unknown we used the planarian eye lineage to address this problem following decapitation neoblasts normally give rise to a large number of eye progenitors facilitating eye regeneration remarkably we found that eye absence alone was not sufficient to induce this response tissue specific eye regeneration was achieved by homeostatic eye progenitor production accompanied by a decreased rate of cell death specifically in the regenerating eye conversely large head wounds were sufficient to increase eye progenitors even in the presence of intact eyes therefore eye absence

is not sufficient or necessary for neoblasts to increase eye progenitor production our findings suggest a target blind model for planarian regeneration in which progenitor production by neoblasts does not depend on feedback from the presence or absence of specific target tissues to be regenerated

the fundamental requirements for regeneration are poorly understood planarians can robustly regenerate all tissues after injury involving stem cells patterning cues and a set of cellular and molecular responses collectively called the missing tissue or regenerative response the missing tissue response has long been considered a fundamental requirement of planarian regeneration follistatin which encodes an extracellular activin inhibitor is required for the missing tissue response after head amputation and for subsequent regeneration we found that follistatin is required for the missing tissue response regardless of the wound context but only causes regeneration failure after head amputation this head regeneration failure involves follistatin mediated regulation of wnt signaling at wounds and is not a consequence of a diminished missing tissue response we found that all tested contexts of regeneration including head regeneration could occur with a defective missing tissue response however at a slower pace our findings suggest that in the absence of major cellular and molecular programs induced by large injuries regulation of wound induced wnt signaling to enable regenerative re patterning along with continuous tissue turnover can mediate successful regeneration in essentially any wound context wnt signaling regulates primary body axis formation across the metazoa with high wnt signaling specifying posterior identity whether a common wnt driven transcriptional program accomplishes this broad role is poorly understood we identified genes acutely affected after wnt signaling inhibition in the posterior of two regenerative species the planarian schmidtea mediterranea and the acoel hofstenia miamia which are separated by 550 million years of evolution wnt signaling was found to maintain positional information in muscle and regional gene expression in multiple differentiated cell types sp5 hox

genes and wnt pathway components are down regulated rapidly after beta catenin rnai in both species brachyury a vertebrate wnt target also displays wnt dependent expression in hofstenia planarian sp5 inhibits wnt dependent expression of trunk genes in the tail promoting separate tail trunk body domains we propose that common regulation of a small gene set hox sp5 and brachyury might underlie the widespread utilization of wnt signaling in primary axis patterning across the bilateria

planarians are bilaterally symmetric metazoans that have the incredible ability to completely regenerate their entire body from a piece as small as 1 279th of a whole animal this amazing regenerative capacity requires a population of stem cells called neoblasts several genes have been identified that are essential for regeneration in the planarian schmidtea mediterranea conservation of most of these genes across the animal kingdom suggests that planarians are an excellent model system to study stem cell biology micrornas are small non coding rna molecules 21 24 nt in length that function by binding to the 3 utrs of mrnas where they prevent translation of the encoded protein or promote mrna degradation in other species mirnas have been shown to be involved in processes as diverse as fat metabolism hematopoiesis apoptosis and the cell cycle to begin studying the role of mirnas in regeneration and stem cell function in planarians we set out to identify mirnas during our experiments we sequenced over 2 400 000 small rnas which allowed us to identify 104 mirna encoding loci in the s mediterranea genome our analysis of sequences from intact regenerating and irradiated planarians has revealed dynamic changes in mirna expression patterns in particular we found that members of the let 7 family of mirnas appear to be expressed in neoblasts and therefore might be important regulators of stem cell function in planarians our sequencing efforts have also identified a second class of small rnas in planarians called pirnas intriguingly in contrast to what is observed in other metazoans in planarians pirna expression is not restricted to the germline but rather appears to be specific to neoblasts therefore pirnas

appear to be regulators of stem cell maintenance and or self renewal in planarians to further study the function of mirnas in regeneration we have cloned cdnas encoding the mirna synthesis machinery depletion of these proteins by rna interference has revealed that a subset of these proteins are required for regeneration homeostasis and proper mirna synthesis these experiments lay the groundwork for functional studies aimed at clarifying the role of mirnas and pirnas in regeneration cell lineage decisions and basic stem cell biology

this classic study of planarian regeneration by the nobel laureate thomas hunt morgan is a must read for students of biology and genetics morgan s experiments explored the fascinating ability of these flatworms to regenerate lost body parts shedding light on the mechanisms of genetic inheritance and cellular differentiation this book is a groundbreaking work in the field of genetics and a fascinating read for anyone curious about the mysteries of life this work has been selected by scholars as being culturally important and is part of the knowledge base of civilization as we know it this work is in the public domain in the united states of america and possibly other nations within the united states you may freely copy and distribute this work as no entity individual or corporate has a copyright on the body of the work scholars believe and we concur that this work is important enough to be preserved reproduced and made generally available to the public we appreciate your support of the preservation process and thank you for being an important part of keeping this knowledge alive and relevant

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